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The Role of Radiologically Guided Fine Needle Aspiration Cytology in The Diagnosis of Renal Masses

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قال تعالى

{الَّذِي خَلَقَنِي فَهُوَ يَهْدِينِ{78} وَالَّذِي هُوَ يُطْعِمُنِي وَيَسْقِينِ{79} وَإِذَا مَرِضْتُ فَهُوَ يَشْفِينِ{80} وَالَّذِي يُمِيتُنِي ثُمَّ يُحْيِينِ{81} وَالَّذِي أَطْمَعُ أَن يَغْفِرَ لِي خَطِيئَتِي يَوْمَ الدِّينِ{82} رَبِّ هَبْ لِي حُكْماً وَأَلْحِقْنِي بِالصَّالِحِينَ}

صدق الله العظيم

سورة الشعراء

DEDICATION

TO ALL MEMBERS OF MY FAMILY, MY EXTENDED FAMILY, AND PARTICULARLY MY FATHER, WHO IS MY HERO IN LIFE.

CONTENTS

Declaration

Dedication

Table of content……i

Acknowledgement……iv

Abbreviation……v

English abstract……vi

Arabic abstract……viii

List of figures……ix

List of tables ……x

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW……1

1.1 Normal anatomy and histology……5

1.1.1 Gross anatomy……5

1.1.2 Normal histology ……5

1.1.3 Blood supply and lymphatic draining……7

1.1.4 Innervations……8

1.1.5 Embryology……8

1.2 Epidemiology ……10

1.3 Risk factors……11

1.4 Pathogenesis ……12

1.5 Clinical features……13

1.6 Imagines……14

1.7 Pathology……..……..14

1.7.1 Non Neoplastic……..….14

1.7.1.1 Renal cyst……..…….…….15

1.7.1.2 Tuberculosis……..…….16

1.7.1.3 Abscess……17

1.7.41. Infarction……..……17

1.7.2 Benign lesions…….……..……18

1.7.2.1 Perirenal lipoma……..18

1.7.2.2 Angiomyolipoma……..18

1.7.2.3 Metanephric adenoma…….....20

1.7.2.4 Mixed epithelial and stromal tumors…….....21

1.7.2.5 Cystic nephroma…….…….....21

1.7.2.6 Oncocytoma…….……22

1.7.3 Malignant tumors.....…….....23

1.7.3.1 Renal cell carcinoma…..……23

1.7.3.2 Conventional real cell carcinoma…….……24

1.7.3.3 Papillary renal cell carcinoma……..……..…26

1.7.3.4 Chromophobe renal cell carcinoma……..……28

1.7.3.5 Collecting duct carcinoma……..……...29

1.7.3.6 Sarcomatoid renal cell carcinoma……..……..…30

1.7.3.7 Carcinoma of the renal pelvis……..…..31

1.2.3.8 Sarcomas……..……..32

1.2.3.9 Wilms' tumor……...…..33

1.8 WHO classification…….34

1.9TNM classification…….34

1.10 Staging and Grading of renal cell carcinoma…..…….34

1.11 Treatment……..…….36

1,12 Prognosis…….……37

OBJECTIVES……..38

CHAPTER TOW

METHODOLOGY……...……39

CHAPTER THREE

RESULTS……...….41

CHAPTER FOUR

DISCUSSION……..…….65

CONCLUTION……..…..70

RECOMMENDATIONS…….71

REFERENCES……..…72

APPENDIX-Questionnaire

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List of Abbreviations

FNAC	Fine Needle Aspiration Cytology.
PTH	Police Teaching Hospital.
RCC	Renal cell carcinoma.
RICK	Radio – isotopes centre of Khartoum.
C.T scan	Computed Tomography scan.
TNM	Tumor, nodes and metastasis system.
U\S	Ultrasonography.
WHO	World Health Organization.

ABSTRACT

background: Renal masses represent 3% of all visceral tumors with high morbidity and mortality rates both in the developed and developing countries. The aim of the study is to evaluate the role of imaging guided fine needle aspiration cytology in diagnosis of renal masses.

Methods: A retrospective study done between 2007-2010 , at Police Hospital , on 52 Sudanese patients with renal masses, diagnosed radiologically. Clinical data and cytological slides were collected from the records. Fine needle aspiration of the renal lesions was done guided by ultrasound in 16 cases and by CT scan in 36 cases. The cytological slides were examined by the candidate and experienced cytopathologist. Histopathological slides were available for only ten cases, examined and correlated by the candidate and experienced histopathologist.

Results: The study included 52 patients. The mean age ± SD was 54.44 ± 15.6 years, the age ranged from 24-88 years with a majority of patients above the age of 40 years (80.8%). Females to male ratio was 1.2:1. Thirty three patients (63.5 %) were from the central regions including Khartoum state. Renal cell carcinoma was most cancer in the central region 23 patients (69.7%). Cytological examination revealed 37 patients with malignant lesions and 15 patients with benign lesions. The ratio between the benign (28.9 %) and malignant (71.1 %) lesions was 1.0:2.5. Five cytological types of renal cell carcinoma were identified. Those were conventional renal cell carcinoma (77.1%), chromophobe renal cell carcinoma (5.7%), metastatic renal cell carcinoma (8.6%), suprarenal carcinoma (5.7%) and squamous cell carcinoma (2.9%). Ten

out of the 52 patients had a histologically confirmed carcinoma, two of which were cytologically diagnosed as benign lesions. For the remaining 42 cases; 15 cases diagnosed as benign lesions and no histopathological examination was done. The next 15 cases cytologically diagnosed as malignant lesions with radiological evidence of metastasis and there for no histopathological examination was done. For the last 12 cases histopathological slides and blocks were not available.

Conclusion: FNAC is a useful technique in evaluating renal masses. It is simple, safe and what made it more useful is the better coordination between radiologist, pathologist and clinicians.

المستخلص

الخلفية: تشكل اورام الكلى حوالى 3% من كل الخبيثات ، حيث تتميز بمعدلات عالية من الامراضية والوفاة في الدول المتقدمة والنامية على حد سواء.

الهدف من هذه الدراسة هو تحديد وتقيم دور الرشف بالابر الدقيقة في تشخيص اورام الكلي .

منهجية البحث: في دراسة ارتجاعية في الفترة من 2007 الي 2010 بمستشفي الشرطة علي 52 مريض سوداني لديهم اورام في الكلي ، تم تشخيصها شعاعيا. تم جمع المعلومات السريرية والشرائح الخلوية من السجلات. تم الرشف بالابر الدقيقة الموجهة بالموجات فوق الصوتية في 16 حالة وفي 36 حالة موجهة بالاشعة المقطعية .الشرائح الخلوية تم تشخيصها بواسطة الباحث واختصاصى خبير في الرشف بالابر. تم جمع الشرائح النسيجية لعشرة حالات ومن ثم تشخيصها ومقارنتها بالشرائح الخلوية بواسطة الباحث واختصاصي خبير في علم الانسجة المريضة .

النتائج: تضمنت الدراسة 52 مريض وكان متوسط الاعمار هو 54.44 ± 16.6 سنة حيث كانت اعمارهم تتراوح ما بين 24– 88 سنة. ابرزت الدراسة الى النسبة العالية للمرضى باورام الكلي للاعمار ما فوق الاربعين سنة (80.8%) . اثبت الدراسة ان عدد الاناث اكثر من عدد الذكور بنسبة 1:1.2. اثبت الدراسة ان 33 مريض (63.5%) يقطنون المناطق الوسطى للبلاد بما فيها الخرطوم، حيث اوضحت الدراسة ان هنالك نسبة عالية من سرطانات الكلي 23 مريض (69.7%) للذين يقطنون هذه المناطق بمعدل 2.5:0.1. بالفحص المجهرى للشرائح تم التعرف على 37 حالة اورام خبيثة ، و15 حالة اورام حميدة بنسبة 2.5:1 ، حيث تم التعرف على 5 انوع من اورام الكلى الخبيثة وهى ، سرطانات خلاية الكلى الصافية 77.1% ، سرطانات ثانوية فى الكلى 8.6% ، سرطانات خلاية الكلى كاره للون 5.7% ، سرطانات الغدة فوق الكلى 5.7% وسرطانات الخلاية الحرشفية 2.9%. لقد تم الفحص النسيجى لعشرة حالات من بين 52 حالة وكانت كلها اورام خبيثة ، بينما بالرشف بالابر كانت هنالك حالتان لم يتطابق التشخيص فيهما . هنالك 30 حالة لم تؤخذ لهم عينات نسيجية منها 15 حالة تم تشخيصها كاورام حميدة و15 حالة اخري أثبت التشخيص بالاشعة ان هنالك انتقال للمرض الي اجزاء اخري من الجسم. هنالك 12 حالة لم نتمكن من ايجاد شرائح نسيجية ولا أنسجة محفوظة لهم.

التضمين: الرشف بالابر الدقيقة الموجهة بالصور الاشعاعية طريقة مفيدة لتقيم افات الكلي وعله وهي عملية بسيطة وسهلة والتشخيص الخلوى سهل مفيد في تحديد الافات . هذه العملية ناجحة في وجود خبرة بالرشف الدقيق والتنسيق بين اختصاصي الاشعة والامراض والمختص السريرى .

List of Figures

Page

Figure **1.** Sex distribution of the study population..... 51

Figure **2**. Benign versus malignant lesions among the study population..... 52

Figure **3**. Sex distribution among patients with renal cell carcinoma in study population..... 53

Figure **4**. Site distribution of renal masses among Study population.....54

Figure **5**. Distribution of the study population according to residence.....55

Figure **6**. Cytological type of benign renal lesions among study population..... 56

Figure **7**. Cytological type of malignant renal lesions among study population..... 57

Figure **8**. Radiologically detected metastatic lesion in the kidney among the study population..... 58

Figure9. Chromophobe RCC 59

Figure 10. RCC; high power 60

Figure 11. RCC; high power.....61

Figure 12. RCC, dyscohesive cells 62

Figure 13. Conventional RCC 63

Figure 14. Conventional RCC 64

LIST of TABLES

Page

Table 1. Age distribution of the study population..... 45

Table 2. Age distribution among patients with renal cell carcinoma..... 46

Table 3. Clinical presentation of renal lesions among the study population..... 47

Table 4. Types of radiology used with benign versus malignant among the study population..... 48

Table 5. Benign versus malignant lesions among the study population in the central region..... 49

Table 6. Correlation between histological and cytological Diagnosis among the study population..... 50

Chapter One

1- INTRODUCTION AND LITRATURRE REVIW

The use of percutaneous large-bore needle biopsy of the kidney has become widespread since its introduction 60 years ago . It is a routine procedure for the evaluation of diffuse renal diseases in most medical centers. Percutaneous fine-needle aspiration biopsy of renal masses has also gained recognition in the last 30 years [1,2]. In our clinical practice , renal lesions are commonly detected by intravenous pyelography , but the latter is a very poor discriminator for type of the lesions . Ultrasonography and CT-scan are useful techniques that can differentiate solid from cystic lesions. Percutaneous fine-needle aspiration biopsy of renal masses can be easily performed under the guidance of Ultrasonography or CT-scan either to identify and evacuate benign cysts or abscesses or to diagnose small renal neoplasm, which may not be so obvious on imaging studies. Early detection of renal cell carcinoma may save lives. In addition , preoperative diagnosis of renal neoplasm by transabdominal fine-needle aspiration biopsy may provide optimal patient management.

In the past decade , the field of radiology has experienced great technological advances .A number of improved imaging techniques, such as computed tomography (CT scan) and Ultrasonography that use powerful computers and produce sectional

images have been developed . They can reliably detect small lesions in the abdomen.[4,5]

Transabdominal fine-needle aspiration biopsy started in Toronto General Hospital in Canada in 1975 [3]. By late 1980s , clinicians started to give preference to the fine-needle aspiration method over other diagnostic procedures because it provides a rapid diagnosis. Therefore, additional laboratory investigation and hospital stay are saved.

The indications for the procedure vary from center to center. This diagnostic procedure is certainly the method of choice in the following settings:

1. Medical contraindications to laparotomy, or a patients refusal of surgery, or the presence of a metastatic disease.
2. Inoperable cancer in which a pathologic diagnosis is required before radiotherapy and / or chemotherapy.
3. Confirmation of a suspected cancer in a patient who is a marginal surgical risk to indicate the need for operation.
4. Confirmation of a suspected localized benign lesion, especially in poor risk patients, thereby obviating laparotomy.
5. Confirmation of a suspected recurrent or metastatic malignant tumor.

6. In cases in which there is a clinical suspicion of more than one type of malignant lesion, including malignant lymphoma.
7. Identification of offending organisms in cases of infection, e.g. an intra abdominal abscess.
8. Staging of a malignant tumor in a patient who has adrenal or liver lesions and/ or enlarged pelvic or retroperitoneal lymph nodes suspected of harboring metastases. [6]

Contraindications to needle biopsy, such, as ileus, bowel distention, uncontrolled coughing, and poor patient cooperation. The method is easy and safe, and the diagnosis is quick. In experienced hands, the procedure is highly accurate in obtaining a pathologic diagnosis, and the clinician can opt to perform the technique without hesitation [7] .

The savings in morbidity, mortality, and health care resources are considered the major advantage of this diagnostic method . The procedure can be performed on an outpatient basis, be readily repeated, be used for multiple lesions, and be done in debilitated patients. In general, the morbidity from transabdominal fine-needle aspiration biopsy is minimal and it far outweighed by the clinical value of the procedure. The possibility of tumor spread along the needle tract following needle biopsy, especially cutting needle

biopsy, has been mentioned in the literature, but the risk of tumor spreading is considered negligible when the fine-needle technique is used .The reliability of this procedure depend on the accuracy of obtaining a representative sample and accuracy of cytomorphological interpretation[7].

1.1 Normal anatomy and histology of the kidney:

1.1.1 Gross anatomy:

The kidney lie in the retroperitoneal position on the posterior abdominal wall, in the superior lumbar region T11_T12. The right kidney is lower than the left. Each kidney weight about 150 gm . The lateral surface is convex; the medial surface is concave. Anterior to the right kidney lie the adrenal gland , the liver , the 2nd part of duodenum ,the right colic flexure . Posteriorly, the diaphragm , 12th rib , the psoas muscle , sub costal (T12) iliohypogastric and ilioinguinal nerves (L1) run downwards and laterally . In the left kidney anteriorly lie the adrenal gland, the spleen, the stomach, the pancreas, and the left colic flexure. Both kidneys are covered by a fibrous capsule (prevent kidney infection); perirenal fat, renal fascia(outer layer of dense fibrous connective tissue that anchor the kidney) and the renal fat ; (external to the renal fascia)[10].

1.1.2 Normal histology:

Each kidney composed of a cortex (the outer part of the kidney) and the medulla (the inner part) . The renal parenchyma is composed of, functional units called the nephron, and connective tissue, the interstitium. There are about 2 million nephron per kidney.

The majority of nephrons lie in the cortex. Each nephron consists of a tuft of anastomosing capillaries called the glomerulus, formed from the afferent arteriole and draining into the efferent arteriole, and a tubular system called the renal tubule. Epithelial cells called podocytes (or visceral epithelium of Bowman's capsule) invest the glomerulus, and are reflected to become continuous with the parietal epithelium of the Bowman's capsule. The Bowman's capsule is the bulbous, distended, closed proximal end of the tubular system and is invaginated by the glomerulus. The space between the glomerulus and capsule is the urinary space. Extending from the capsule is the proximal tubule, which is lined by tall cuboidal-to-columnar epithelial cells containing many mitochondria and a prominent brush border. The proximal tubule is the longest portion of the tubular system and is made up of convoluted proximal and distal straight (pars recta) segments. The pars recta descends into the medulla, where it forms the U-shaped loop of Henle. The latter reenters the cortex within which it forms the straight and convoluted segments of the distal tubule. The distal tubule, at about the junction between its two segments, runs close to the glomerular hilum and forms a specialized segment called the macula densa The distal tubule is lined by cuboidal epithelium that lacks brush border. Then it drain into the collecting duct, minor calyces, major calyces and into the renal pelvis; which lined by transitional urothelial cells.

The mesangium consists of cells and matrix; it fills the space between the glomerular capillaries and extends with the vascular pedicle to the extraglomerular space. The mesangial cells have a contractile function, they insert with microfilaments to the glomerular basement membrane. The contraction of the mesangial cells controls and enables the high glomerular filtration pressure of 35–50 mmHg.[11]

1.1.3 Blood supply:

The kidneys receive blood from the right and left renal arteries, which branch directly from the abdominal aorta. Despite their relatively small size, the kidneys receive approximately 20% of the cardiac output.

Each renal artery branches into segmental arteries, dividing further into interlobar arteries which penetrate the renal capsule and extend through the renal columns between the renal pyramids. The interlobar arteries then supply blood to the arcuate arteries that run through the boundary of the cortex and the medulla. Each arcuate artery supplies several interlobular arteries that feed into the afferent arterioles that supply the glomeruli.

The interstitum (or interstitum) is the functional space in the kidney beneath the individual filters (glomeruli) which are rich in blood vessels. The interstitum absorbs fluid recovered from urine. Various conditions can lead to scarring and congestion of this area,

which can cause kidney dysfunction and failure. After filtration occurs the blood moves through a small network of venules that converge into interlobular veins. As with the arteriole distribution the veins follow the same pattern, the interlobular veins provide blood to the arcuate veins then back to the interlobar veins which come to form the renal vein exiting the kidney for transfusion for blood. (11)

1.1.4 Innervation:

The kidney and the nervous system communicate via the renal plexus , whose fibers course along the renal arteries to reach the kidney. Input from the sympathetic nervous system triggers vasoconstriction in the kidney, thereby reducing renal blood flow. The kidney is not thought to receive input from the parasympathetic nervous system. Sensory input from the kidney travels to the T10-11 levels of the spinal cord and is sensed in the corresponding dermatome. Thus, pain in the flank region may be referred from the kidney.[12]

1.1.5 Embryology:

The urogenital system develops from the intermediate mesoderm, the mesodermal epithelium (mesothelium) of the peritoneal cavity, and the endoderm of the urogenital sinus .

The nonfunctional, rudimentary pronephric develop early in week 4. But they degenerate, leaving behind the pronephric ducts which run to the cloaca . These ducts will remain for other kidneys. The mesonephroi develop later during week 4, serving as temporary excretory organs. The functional metanephroi or permanent kidneys develop early in week 5. They are functional by week 11-13 and excrete urine into the amniotic fluid. This excretion continues during fetal life and the fetus swallows this urine mixed in the amniotic fluid. It is then absorbed in the stomach and duodenum to the blood for transport to the placenta and disposal. If renal agenesis or urethral obstruction occurs, oligohydramnios results. If esophageal or duodenal atresia occurs, then polyhydramnios results.

The metanephros develops mesodermally from the metanephric diverticulum or ureteric bud which is a dorsal outgrowth from the mesonephric duct near the cloaca. Its stalk gives rise to the ureter. Its cranial end to the renal pelvis , its first 4 generations of tubules to the major calyces, its second 4 generations to the minor calyces and the remaining generations of tubules to the collecting tubules. The metanephric diverticulum or ureteric bud penetrates the metanephric mesoderm in the caudal part of the Nephrogenic cord and stimulates the formation of the metanephric mass or cap.

The metanephric mesoderm gives rise to the nephrons (glomerulus, Bowman's capsule, proximal convoluted tubule, loop of Henle and distal convoluted tubule). The cortex of the kidney in the newborn contains mostly undifferentiated mesenchyme; the nephrons continue to develop several months after birth.

The kidneys are first located in the pelvis, ventral to the sacrum but gradually ascend to the abdomen. They reach the adult position by week 9 having touched the suprarenal glands This is due to the disproportionate growth between the lumbar and sacral regions: the sacral region grows faster than the lumbar region.[13]

1.2. Epidemiology:

In 2010, approximately 58,000 people were diagnosed and about 13,000 will die from RCC in the United States (US) [59] ; worldwide, there were an estimated 270,000 cases and 116,000 deaths in 2008.[60] The incidence varies widely from region to region with the highest rates observed in Scandinavia and North America. [61] Although the incidence is lower in Africa , whites and blacks appear to be equally affected in the United States. [62]

The incidence of RCC in the US has increased over time. [63,64] Between 1975 and 1995 , the incidence rates per 100,000 person/years increased by 2.3, 3.1, 3.9 and 4.3 percent annually for

white men, white women, black men , and black women , respectively [65]. More recent data from 1997 to 2007 showed a similar trend with 2.6 percent increased yearly incidence [66].

During this period , the size of tumors at presentation has decreased and more patients are presenting with stage I disease. (64,67) In an analysis of over 29,000 cases from the Surveillance, Epidemiology and End Results (SEER) database , this increased incidence has been associated with a steady decrease in the average size of tumors at presentation (6.7 versus 5.9 cm in 1988 and 2002, respectively). (64)

In Sudan, according to reports derived from the department of medical statistic and registration of Radioisotopes centre of Khartoum renal cell carcinoma is estimated to account for 2.2% of all cancer cases(9). The tumors occur most often in older individuals, usually in the sixth and seventh decades of life, showing a male preponderance in the ratio of 2 to 3:1.

1.3. Risk Factors:

Cigarette smoking and obesity are the strongest known risk factors. Hypertension and a family history of the disease are also risk factors. Patients on dialysis will acquired cystic disease of the kidney showed a 30 times greater risk than in the general population for developing RCC (68). Exposure to asbestos , polycyclic

aromatic hydrocarbons , gasoline has not been shown to be consistently associated with RCC risk. [69] Patients with certain inherited disorders such as von Hippel-Lindau disease , hereditary papillary renal cancer , a hereditary Leiomyoma RCC syndrome and Birt-Hogg-Dubé syndrome, show an enhanced risk of RCC. [70] Also, patients with sickle cell trait are predisposed to develop Renal medullary carcinoma. Hysterectomy is associated with an approximately doubled risk. Hormonal factors or injury of the ureter during surgery were considered as possible causes.[71]

1.4. Pathogenesis:

Changes (mutations) in genes:

1.4.1. Inherited gene mutations:

Certain inherited DNA changes can lead to conditions running in some families that increase the risk of kidney cancer. For example, the Von Hippel-Lindau (VHL) gene is a tumor suppressor gene. When the VHL gene is mutated, it no longer function to suppress abnormal growth, and kidney cancer is more likely to develop. The genes linked to hereditary leiomyoma and renal cell carcinoma carcinoma (the FH gene) and Birt-Hogg-Dube syndrome (the FLCN gene) are also tumor suppressor genes, and inherited changes in these genes also lead to an increased risk of kidney cancer. People with hereditary papillary renal cell carcinoma have inherited changes in the MET oncogene that cause it

to be "turned on" all the time. This makes the person more likely to develop papillary renal cell carcinoma.

1.4.2. Acquired gene mutations:

About 3 out of 4 people with sporadic (non-inherited) clear cell renal cancer have changes in the VHL gene that cause it not to function properly. These changes were acquired during life rather than being inherited. Other gene changes may also cause renal cell carcinomas. Researchers continue to look for these changes. Progress has been made in understanding how tobacco increases the risk for developing renal cell carcinoma. As the lungs absorb many of the cancer-causing chemicals in tobacco smoke into the bloodstream. Because the kidneys filter this blood, many of these chemicals become highly concentrated in the kidneys. Obesity, is another cause of this cancer, due to alter often in the balance of some of the body hormones.

1.5. Clinical Features of Kidney Cancer:

The three classic diagnostic features of renal cell carcinoma are costovertebral pain, palpable mass, and haematuria, but these are seen only in 10% of cases. The most reliable of the three is haematuria, but it is usually intermittent and may be microscopic; thus the tumor may remain silent until it attains large size. At this time, it gives rise to generalized symptoms, such as fever, malaise, weakness, and weight loss.

In current times, however, many of these tumors are being discovered in asymptomatic state by incidental radiological studies (e.g., ultrasound or CT scan) usually performed for nonrenal indications. Renal cell carcinoma may produce a number of paraneoplastic syndromes due to abnormal hormones production, including polycythemia, hypercalcemia, hypertension, hepatic dysfunction, feminization or masculinization, Cushing syndrome, eosinophilia, leukemoid reactions, and amyloidosis. [8] One of the common characteristics of this tumor its tendency to metastasize widely before giving rise to any local symptoms or signs.

1.6. Imaging tests:

Imaging tests such as x-rays , magnetic fields, or radioactive substances are helpful to find out whether a suspicious area might be cancerous, to learn how far cancer may have spread, and to determine if treatment has been effective.

Chest x-rays and bone scans, are more often used to help determine if the cancer has spread (metastasized) to other parts of the body.

1.7 Pathology:

1.7.1. Non neoplastic mass lesions:

Common nonneoplastic lesions that may present as a space-occupying mass include renal cyst, tuberculosis, abscess and infarct.

The use of modern imaging techniques, such as Ultrasonography and CT-scan, aided by percutaneous fine-needle aspiration biopsy has virtually eliminated the need for exploration of these nonneoplastic lesions.

1.7.1.1. Renal Cysts:

Cysts are the most commonly aspirated renal lesions. A multitude of cystic lesions involve the kidneys. They may be hereditary or acquired. Most renal cysts are asymptomatic, except for adult polycystic disease. However, rupture , hemorrhage or torsion may occasionally call attention to the lesions. The most common cystic lesion of the kidney encountered in the practice of aspiration biopsy is the simple cyst. 50% of individuals of 50 years of age or older may have one or more simple cysts . They contain clear yellow fluid and displace renal parenchyma. Renal cell carcinomas may also undergo cystic degeneration, frequently with hemorrhagic contents in their cavities. In fact, at least one-third of all renal cysts with hemorrhagic contents are actually cystic carcinomas. It is, therefore, important to aspirate renal cysts of a debatable nature, detected by imaging techniques, for the purpose of diagnosis. Cytologic examination of the aspirated fluid contains few tubular cells with round nuclei. There are also scattered macrophages , often with abundant, foamy cytoplasm. In some cases, numerous hemosiderin-

laden macrophages are present, indicative of prior hemorrhage into the cavity of the cyst. In occasional cases, irritated epithelial cells and reactive macrophages may mimic malignancy. [14,15] However, they are usually are seen and intermingled with many recognizable benign cells, and do not form large tissue fragments, as in carcinomas, and there is absence of necrotic cells and debris. Ultrasonography, which demonstrates a smooth lining of the cystic cavity, confirms the diagnosis of a benign cyst[16].

1.7.1.2 Tuberculosis:

Renal tuberculosis was a common disease in the past but is now in Africa, there are few reports of renal tuberculosis and rare in North America. It is hematogenous in origin, and the infection usually originates from foci in the lung. The lesion of renal tuberculosis may vary from minute areas of ulceration near the tips of papillae to huge cavitating masses. The infection may be unilateral or bilateral. Cytologic findings are essentially the same as those of tuberculous lesions elsewhere. The aspirate preparations contain lymphocytes, macrophages, multinucleated giant cells and epithelioid cells. Necrotic debris is usually found and Ziehl-Neelsen stain may identify acid fast bacilli.

1.7.1.3. Abscess:

Renal abscesses are seen in patients with acute pyelonephritis or as part of the systemic inflammatory process. The patients with renal abscesses experience ipsilateral costovertebral angle pain and tenderness, chills and fever, and sometimes pyuria. The infection may be limited to the renal pelvis or may involve the entire kidney. Fine-needle aspiration biopsy can identify and evacuate the abscess.[17] The aspirates consist of purulent exudate and contain abundant neutrophilic inflammatory cells and nuclear debris. If the biopsy is performed because of suspected infection or when purulent material is aspirated, the specimen should be sent for microbiologic studies, including Gram and Ziehl-Neelsen stains, and for aerobic, anaerobic, tuberculous and fungal cultures.

1.7.1.4. Infarct:

Infarction of the kidney is caused by occlusion of one renal artery that supplies the infarcted area. Occlusion of the renal artery commonly results from arteriosclerosis, thrombosis or atheromatous embolism. Occlusion of the major renal artery usually causes ischemic necrosis in several renal lobules and rarely leads to total infarction of the kidney. Collateral vascular supply from capsular or adrenal vessels usually suffices for viability of irregularly defined areas of renal cortex. The aspirate preparations contain many dying

tubular cells with pyknotic nuclei; scattered necrotic tubular cells appearing as ghost cells; and necrotic cellular debris. Very few inflammatory cells are seen.

1.7.2. Benign tumors:

Benign tumors of the kidney make up less than 5% of all renal neoplasms. [8] They can arise from the epithelial elements or nonspecific stroma. Common benign tumors of the kidney include perirenal lipoma, angiomyolipoma and Oncocytoma. Uncommon benign tumor of the kidney includes metanephric adenoma and mixed epithelial and mesenchymal tumor (adult mesoblastic nephroma). [18]

1.7.2.1. Perirenal Lipoma:

Perirenal lipomas arise in the fat normally present in the perirenal regions. They may become huge. They are histologically similar to lipomas in any other part of the body. The aspirate preparations contain fragments of adipose tissue and scattered fat cells. Also encountered are many free oil droplets that are produced when the fat cells burst as a result of the aspiration procedure. Taken together, the cytologic findings, the CT-scan appearance, and the feeling of empty sensation during aspiration biopsy establishes the diagnosis of lipoma. [18]

1.7.2.2. Angiomyolipoma

Angiomyolipoma is an uncommon soft tissue tumor involving the kidneys, liver and other organs. Long believed to be a benign

hamartoma composed of thick-walled blood vessels, smooth muscle and mature adipose tissue, angiomyolipoma is now considered part of a family of neoplasms derived from perivascular epithelioid cells (PEComas), including also clear cell sugar tumor of the lung, clear cell myomelanocytic tumor of the falciform ligament, abdominopelvic sarcoma of perivascular epithelioid cells and lymphangioleiomyomatosis. [19,20] The neoplastic cells of PEComas are characterized by expression of muscle and melanocytic (HMB-45) markers. [21]

Angiomyolipoma occur most commonly in middle aged and older women but may be seen in younger persons. They may be multiple or bilateral. Approximately one-third of the patients with renal angiomyolipoma are associated with tuberous sclerosis, a disorder involving gliosis of the brain, adenoma sebaceum of the face, and multiple hamartomas in the liver, pancreas and the kidney. The incidence is higher in cases of multiple or bilateral angiomyolipoma. About 80% of the patients with severe form of tuberous sclerosis have renal tumors of this type. At CT-scan, angiomyolipoma typically appears as a well- marginated, cortical, predominantly fat-attenuated mass with heterogeneous soft-tissue attenuation interspersed throughout the lesion [22]. In tissue sections, the hyperchromatism, pleomorphism, and moderate mitotic activity of the tumor cells may result in a

mistaken diagnosis of leiomyosarcoma, but the clinical course of this tumor is almost always benign. [19]

The use of fine-needle aspiration biopsy in establishing the diagnosis of this tumor has been reported [23,24]. The preoperative diagnosis of angiomyolipoma may affect the surgical approach [23,25]. The cytologic diagnosis of angiomyolipoma can be difficult and is often missed in inexperienced hands. The three components seen in tissue sections are either not seen or unusual looking in aspirate preparations. Because there is no endothelial proliferation of the blood vessels within the tumor, endothelial components are not seen in aspirates. In some cases, fat cells are not seen in aspirates, because solitary and small clusters of fat cells tend to burst during the aspiration procedure.

The cytologic diagnosis of angiomyolipoma is therefore often difficult. Awareness of the variable cytologic appearances of neoplastic cells , the positive HMB-45 immunostain and the CT-scan finding of a fat-containing low-density lesion may establish the diagnosis.

1.7.2.3 .Metanephric Adenoma:

Histology shows tightly packed small tubules made up of simple cuboidal epithelium accompanied by scanty stroma. Fine-needle aspiration cytology of metanephric adenoma has been

reported. [26] Aspirate preparations show numerous loosely cohesive small cells with minimal cytoplasm and small and bland nuclei forming vague tubules. An occasional row of cells survives the smearing artifact.

1.7.2.4. Mixed Epithelial and Stromal Tumor :

This tumor used to be called "adult mesoblastic nephroma" until 2001 when a cytogenetic study[27] determined that it bears no relationship to childhood mesoblastic nephroma. Histologically, the tumor is composed of tubules scattered in a fibrotic stroma composed of spindly nuclei with eosinophilic fibrillary cytoplasm. Aspirate shows bundles of fibroblast-like spindle cells with bland nuclei and abundant fibrillary cytoplasm. The entrapped tubules are difficult to find.

1.7.2.5. Cystic Nephroma:

Histology shows multiple cysts in an ovarian-type cellular spindle cell stroma. The cysts are lined by flat to "hobnail" cells. The aspirate preparations show serous cyst fluid containing scattered atypical epithelial cells and fibrous stroma composed of spindle cells. The atypical epithelial cells are the hobnail cells from the lining of the cyst.

1.7.2.6. Oncocytoma:

Oncocytomas of the kidney, first described in 1942, was ignored in the literature until 1976 when Klein and Valensi [28] published 13 additional cases. Oncocytoma, initially thought to be derived from proximal tubules, is now believed to be derived from the intercalated ducts. Oncocytomas are asymptomatic and usually discovered incidentally during work-up for other problems or at autopsy. [29] The increasing use of imaging technique sled to the discovery of more oncocytomas. The preoperative diagnosis of oncocytoma by aspiration biopsy has been reported.[30,31] Although most oncocytomas behave in a benign fashion, a few tumors were reported to be invasive and capable of metastasis. [32] It is possible those cases may be misdiagnosed as renal cell carcinomas. Histological examination shows that the tumors are composed of epithelial cells arranged in a cord, tubular or alveolar pattern, displaying uniform , round nuclei and granular, acidophilic cytoplasm due to the presence of abundant, large mitochondria. The aspirate preparations shows tumor cells forming small cohesive groupings, sheet and solitary cells . The cells are polygonal, with an abundance of well-defined, granular cytoplasm and relatively uniform, round or ovoid nuclei. The nuclei are either centrally or eccentrically located. The nucleoli are inconspicuous or small, and the chromatin is finely

granular. Cytomorphologically, they may resemble hepatocytes. It is, therefore, important to ascertain that the needle tip is definitely in the lesion when aspiration biopsy of the tumor is performed on the right kidney and, especially, when a transhepatic approach is used . Occasionally, renal cell carcinomas containing granular cells may have areas morphologically similar to oncocytoma. Aspiration biopsy and tissue core-needle biopsy may lead to an erroneous diagnosis of oncocytoma. Vimentin immune -stain may resolve this diagnostic problem. Vimentin is negative in oncocytoma and positive in renal cell carcinoma

1.7.3. Malignant Tumors:

Primary malignant tumors of the kidney constitute 2 _ 3% of human cancers and account 85% of renal cancer in adults [32] . Malignant tumors, on the other hand, are of great importance clinically and deserve considerable emphasis. By far the most common of these tumors is renal cell carcinoma, followed by Wilms tumor and finally urothelial tumors of the calyces and pelvis. [32]

1.7.3.1. Renal Cell Carcinoma:

Renal cell carcinomas are the most common tumor of the kidney and comprise 80% of all renal neoplasms. They arise from proximal tubular cells (conventional type); distal tubular cells (papillary type); intercalated duct cells (chromophobe type); and

collecting duct cells of renal medulla (collecting duct carcinoma). These neoplasms occur twice as often in men as in women and are usually not discovered until they are sufficiently advanced to cause either a flank mass or haematuria.

The average age at diagnosis is 50 to 60 years. They metastasize mainly through the bloodstream but also by the lymphogenous route. Lung and bones are the most common sites for metastasis. About one third of the patients have distant metastases at initial presentation. Some of the metastases occur before the primary lesion is discovered, whereas other metastases appear many years after the primary tumor has been discovered incidentally by chest radiography, without known primary tumor at the time of investigation, were renal cell carcinoma.

1.7.3.2. Conventional Renal Cell Carcinoma:

Conventional renal cell carcinoma comprised 68% of malignant renal tumors in the Memorial Sloan-Kettering Cancer Center study, [33] with a male : female ratio of 1.7–2:1. The age of presentation ranged from 34 to 90 years (mean 61 years). The putative cell of origin is the proximal convoluted tubules. Conventional renal cell carcinoma can be distinguished from proximal tubular epithelium by the well-defined cell borders in the former and invisible cell borders resulting from interdigitating cell membranes in the latter. [34]

Conventional renal cell carcinomas are composed of clear cells and granular cells in various proportions.

Conventional clear cell renal cell carcinoma:

Histologically , clear cell renal cell carcinoma is composed of clear cells arranged in solid sheets, cords, tubules or papillary patterns. The neoplastic cells have an abundant clear cytoplasm that may appear foamy or vacuolated and have centrally located, round or ovoid nuclei. The vacuolated cytoplasm contains lipid or glycogen .

The morphology in aspirate preparations is variable, single cells, small loose cohesive groups, or sheet arrangements and in papillary fronds with a fibro vascular cores. The diagnosis of renal cell carcinoma should be based on finding cells in clusters and the finding of frequent prominent nucleoli. [33- 35]

Conventional granular cell renal cell carcinoma:

The aspirates of predominantly granular cell conventional renal cell carcinoma are more difficult to interpretate, because cells with granular cytoplasm are present in oncocytoma, [30] eosinophilic chromophobe carcinoma [36,37], papillary renal cell carcinoma, proximal convoluted tubules or hepatocytes.

Cytologically, conventional granular cell renal cell carcinoma occur in loose and cohesive grouping . They have moderate amounts

of granular, often well-defined cytoplasm and large , centrally located, round nuclei . This may cause a diagnostic problem if a transhepatic approach is used for aspiration biopsy of the right kidney . Therefore aspirate preparations should be carefully examined as it may be mistaken as hepatocytes. Conventional granular cell renal cell carcinoma often has focal clear cells and immunostaining for vimentin is positive for conventional granular cell renal cell carcinomas, but negative for hepatocytes and oncocytomas.

1.7.3.3. Papillary Renal Cell Carcinoma:

Papillary renal cell carcinoma is the second most common (7–14%) renal cell carcinoma[32] . The prognosis is better than conventional renal cell carcinoma , the 5-year disease free survival rate being 79–92% [32]. Papillary renal cell carcinoma has a broad morphologic spectrum, ranging from papillary , papillary-trabecular to papillary-solid. The solid variant contains the same genetic alterations as other papillary renal cell carcinomas. [38] Papillary renal cell carcinoma is subdivided into Type 1 and Type 2 . Type 1 is more indolent than Type 2. Type 2 tumors are more common in patients younger than age 40, and present with larger tumor size and at a more advanced stage than were Type 1 tumors. [39]

Type 1 papillary renal cell carcinoma:

Histologically , this subtype consisted of papillae and tubular structures which are covered by simple cuboidal epithelium, with small bland nuclei and pale cytoplasm and Furhman grade 1 nuclei , frequent glomeruloid papillae, foamy macrophages in papillary cores, and psammoma bodies. Cytokeratin 7 is expressed in most cases of this subtype.

The aspirate preparations show cohesive, partially opened , papillary structures with fibrovascular cores in a background of macrophages . Hemosiderin-laden epithelium was a frequent finding in the cases reported. [40,41] Occasionally , the aspirate consists of many small groupings with a connective tissue cores , covered by small tumor cells with scanty granular cytoplasm and without any papillae.

Type 2 papillary renal cell carcinoma:

Histologically , this subtype consisted of papillae covered by pseudostratified epithelium composed of larger , more atypical cells with abundant eosinophilic cytoplasm with Furhman grade 2–4 nuclei and nucleoli are more prominent. Cytokeratin 7 is not expressed in this subtype .

In the aspirate preparations , loosely cohesive papillary structures are found within a background of individual isolated tumor cells removed by the force of smears.

1.7.3.4. Chromophobe Renal Cell Carcinoma:

Chromophobe renal cell carcinoma , previously thought to be seen only in animals , was recognized in human by Thoenes *et al* in 1995 [43]. The prognosis is much better than other types of renal cell carcinoma. Chromophobe renal cell carcinomas account for about 4–6% of all renal tumors. Histologically , there are two variants [44]. In the typical variant , the majority of the tumor cells have abundant cytoplasm with a perinuclear halo of fine reticular texture , outlined by a thick and eosinophilic cell border. In the eosinophilic variant , the majority of the tumor cells are smaller and have markedly eosinophilic cytoplasm , with only focal areas showing perinuclear halos. Histochemically, the tumor cells generally show a diffuse and strong reaction for Hale's colloidal iron stain . Ultrastructurally , the cytoplasm of the tumor cells with a perinuclear halo is filled with microvesicles. Fine-needle aspiration cytology of chromophobe renal cell carcinoma has been reported. [37,44]

In the aspirate preparations, typical chromophobe renal cell carcinoma presents as dyscohesive single tumor cells with abundant cytoplasm and perinuclear halos filled with variable-sized vacuoles.

The nuclei are pleomorphic hyperchromatic with irregular membrane and indistinct nucleoli. Many tumor cells are binucleated . The eosinophilic variant may lack the diagnostic cells with perinuclear halos in the aspirate and may look like oncocytomas or conventional granular cell renal cell carcinoma. [37]

1.7.3.5. Collecting Duct Carcinoma of Renal Medulla:

Collecting duct carcinoma is rare and constitutes < 1% of renal epithelial tumors. It was not recognized as a clinicopathologic entity until 1986. [45] It develops in younger patient , with a mean age of 34 years. [46] It is aggressive; more than half of the patients have metastasis at the initial presentation. Typical collecting duct carcinoma consists of a grossly infiltrative neoplasm centered in the renal medulla. The usual histologic pattern is that of a tubular or tubulopapillary carcinoma within desmoplastic stroma and less commonly , papillary architecture . Origin in the collecting duct is suggested by the tumor's medullary location and dysplasia of the epithelium in the collecting ducts adjacent to the tumor.

Fine-needle aspiration cytology of collecting duct carcinoma has been reported. [47,48] In the aspirate preparations , collecting duct carcinoma of the tubular type presents as cohesive sheets of epithelium with well-defined dense cytoplasm and hyperchromatic coarse granular nuclei with 1–2 distinct nucleoli. Collecting duct

carcinoma of the papillary type is difficult to be distinguished from papillary renal cell carcinoma except for the anatomic site of renal medullary tumor as seen on CT-scan.

1.7.3.6. Sarcomatoid Renal Cell Carcinoma:

Sarcomatoid renal cell carcinoma is high grade de-differentiation tumor of other types of malignant renal cell neoplasms. The tumor shows marked proliferative activity in growth kinetic studies and is usually associated with a poor patient survival, best predicted by staging. Histologically, the tumor is composed of sheets of malignant spindle cells that have immunohistochemical and ultra- structural features of both stromal and epithelial cells, and may contain myxoid areas containing osteoclast-like giant cells or pleomorphic sarcomatoid spindle cells resembling rhabdomyoblasts . Fine-needle aspiration cytology of sarcomatoid renal cell carcinoma has been reported.[49] In the aspirate preparations , tumor cells occur in non- cohesive as well as cohesive groupings. They have ovoid, elongated , or spindle-shaped nuclei and poorly defined cytoplasm , neither vacuolated nor foamy. The cytologic feature of these tumor cells with good intercellular cohesion is helpful in differentiating this tumor from sarcomas, which have poor intercellular cohesion.

Cytologic grading of renal cell carcinomas based on the degree of nuclear anaplasia has been described in the literature as of

prognostic value. [50] However attempts to reproduce the results have not been uniformly successful. [51] It appear s that cytologic grading was most reliable for high-grade tumor s and was inaccurate as the differentiation improved. [50] The cytologic diagnosis of renal cell carcinoma of this type is often missed by inexperienced examiners.

1.7.3.7. Carcinomas of the Renal Pelvis:

Carcinomas of the renal pelvis are uncommon tumors and are predominantly Of the urothelial cell type. The remainders are either squamous cell carcinoma or adenocarcinomas. Urothelial carcinomas can be either papillary or nonpapillary. Most cases are seen in adults. They often diffusely involve the entire renal pelvis. Urothelial carcinomas of the nonpapillary type can spread massively into the renal parenchyma. It is not rare for urothelial carcinomas of the renal pelvis to have areas showing differentiation into adenocarcinomas or squamous cell carcinoma. Pure squamous cell carcinomas of the renal pelvis are rare tumors and are commonly associated with kidney stones and infection. However , metastatic tumors from urothelial carcinomas with some squamous cell carcinoma differentiation may appear as squamous cell carcinoma in metastatic sites. Adenocarcinomas of the renal pelvis are also rare tumors. Like squamous cell carcinomas, they are commonly associated with kidney stones and infection.

In the aspirate preparations, tumor cells derived from papillary urothelial carcinomas are characterized by the so-called “cercariform ” cells , a term coined by Powers and Elbadawi.[52] to describe tadpole-shaped cells with ovoid nuclei and long forked cytoplasmic tails. The cercariform cells often present as solitary cells or as cohesive fragments around a vascular core. The tumor cells from non papillary urothelial carcinoma are generally larger and have round , ovoid or irregular-shaped nuclei with high nuclear /cytoplasmic ratio in solitary cells and in cohesive groupings . The tumor cells from poorly differentiated urothelial carcinoma . Urothelial carcinoma are dyscohesive with bizarre nuclei or multinucleation and may require immunohistochemistry using CK7+/ CK20+ and uroplakin to confirm its urothelial nature. Tumor cells from squamous cell carcinomas are generally of the keratinizing type , with pyknotic nuclei and dense, sharply demarcated, often orangeophilic cytoplasm. The cytological features of adenocarcinomas of the renal pelvis do not differ from those o f the stomach or the lung.

1.7.3.8. Sarcomas:

Primary sarcomas of the kidney are rare and constitute approximately 2% of all malignant neoplasms of the kidney. Leiomyosarcomas are by far the most common sarcoma of the kidney. Other sarcomas are rarely seen. The typical cytological

features of these sarcomas are those of spindle cell with atypical nuclei, multinucleation, and presence of mitosis. The chromatin pattern is unusually fine for such an aggressive neoplasm and nucleoli are rarely seen. Differentiation of renal sarcoma from RCC may be difficult if only the sarcomatoid component of the RCC is aspirated. The presence of positive staining for keratin in the spindle cells, as well as a recognizable epithelial components favors the diagnosis of sarcomatoid RCC [53].

1.7.3.9. Wilms' Tumor:

Wilms' tumors are the most common renal malignancy of infancy and children and rarely occur in adults. [54-56] At least 50% of the cases occur before the age of 3 years and 90% before the age of 10 years. The first indication of this tumor is usually the presence of a large mass in the abdomen. Approximately 25% of patients have metastases to lymph nodes , lungs and liver when first diagnosed. Spread to other organs is rare , even in advanced cases. Establishing the pre -operative pathologic diagnosis is important for optimal patient management [57]. For patients with bulky tumors and vascular invasion , preoperative radiation and chemotherapy are strongly recommended. In Wilms' tumors the occurrence of pulmonary metastases does not necessarily indicate a bad prognosis , but aggressive multimodal therapy is certainly needed [58]. Fine-needle

aspiration biopsy, in addition to establishing a primary diagnosis, can provide information on tumor recurrence and metastases and facilitate treatment decision. Histological examination shows that this tumor contains elements of embryonal epithelium resembling tubules or glomeruli , elements of sarcoma, and undifferentiated tumor cells. The aspirate preparations contain tumor cells in loose groupings , in cohesive clusters , and as solitary cells. They are relatively small and may be in an organoid arrangement with common cell borders or rosette formation. They have round , ovoid , elongated or spindle-shaped nuclei and no recognizable cytoplasm. A necrotic diathesis may be present. (54)

1.8. WHO Histological Classification of Tumors of The Kidney:

The WHO classified renal tumors according to epithelial and mesenchymal (see appendix).

1.9. TNM classification :

The TNM classified tumors according to tumor size, lymph node involvement and distant metastasis (see appendix).

1.10. Stages and grading of Renal Cell Carcinoma:

1.10.1. Staging:

An important prognostic predictor for any type of cancer is the clinicopathologic stage. A clinicopathologic stage describes the cancer developmental phase, and is established according to several criteria :

the tumor size , the cancer location (if the cancer is present in one or both kidneys) , and the cancer extent. [72]

Stage I : In this stage , the cancer is confined to the kidney , and the tumors measures around 7 centimeters.

Stage II : In this stage , the has spread to the fat tissue around the kidney, and the tumor is larger than 7 centimeters.

Stage III : In this stage cancerous cells confined to the kidney, but the cells may enter the lymph system and invaded one adjacent lymph node or spread to the adrenal gland , fat tissue and fibrous tissue that encapsulate the kidney or the cells may spread to the main blood vessel (renal vein) that carries clean blood from the kidneys or to the main blood vessel that carries blood from the lower parts of the body to the heart (inferior vena cava).

Stage IV: The most advance stage of renal cell carcinoma. Cancerous cells have spread to the distant parts of the body; such as spread beyond the fibrous tissue that surrounds the kidney, in several nearby lymph nodes and to adjacent organs such as bowel, pancreas, or lungs. [72]

1.10. 2. Fuhrman Grade:

The most popular and used widely system for grading renal cell carcinoma is a nuclear grading system described in 1982 by Fuhrman et al. Currently, the Fuhrman grading system is most

widely used by pathologist in Europe and United States; this system categorizes renal cell carcinoma with grades 1, 2, 3, and 4 based on nuclear characteristics and represent one of the most significant prognostic variables in patients with all stages of renal cell carcinoma. Grade1; by using the 10x objective, the nuclei of the tumor cells are small (< 10 µm), hyperchromatic, and round (resembling mature lymphocytes), with no visible nucleoli and little detail in chromatin. Grade 2; by using the 10x objective, the nuclei of the tumor cells are slightly larger are (15 µm) looking with finely open chromatin but small, inconspicuous nucleoli. Grade 3; by using the 10x objective, the nuclei of the tumor cells are slightly larger are (20 µm in size) and may be oval in shape, coarsely granular chromatin. The nucleoli are easily unequivocally recognizable. Grade 4; the nuclei are pleomorphic with open chromatin or hyperchromatic and single or multiple macronucleoli. [72]

1.11. Treatment :

Surgery is the primary treatment for nonmetastatic kidney cancer. Surgical removal is the best choice for tumors that confined to the kidney (T1 and T2 cancers), for T3a tumors that have perforated into the fatty tissue around the kidney, and for T3b and T3c tumors that have extended into the venous system. Several non-surgical alternatives are available for patients who are unsuitable for surgical

treatment who are unwilling to have surgery, like arterial embolization, in which the blood supply to the tumor or to the entire kidney is blocked. Radiation therapy is not effective for kidney cancer except to palliate the pain who have bone metastases. Chemotherapy also has not been effective in treating this disease , although recent clinical trials show some promise. A new agent, sorafenib tosylate tyrosine kinase inhibitors, which inhibit angiogenesis, the growth of blood vessels, induced by the cancer can help.[72]

1.12. Prognosis:

The average 5 – years survival rate of the patients with renal cell carcinoma is about 45 % _ 70 % in the absence of distant metastases. With renal vein invasion or extension in to the perinephric fat, the figure is reduced to approximately 15 % _ 20%.

OBJECTIVES

General objectives :

To study cases with renal masses in the study area from January 2007 to December 2010, with the objective to evaluate the role of the use of under guidance fine needle aspiration cytology in the diagnosis of renal masses.

Specific Objectives:

1/ To detect the accuracy of guided fine needle aspiration cytology in the diagnosis of renal masses.

2/ To correlate the cytological diagnosis with the histological one.

Chapter Two

2- MATERIAL AND METHODS

2.1. Study design:

The study is descriptive, retrospective recorded data - based study.

2.2. Study area:

The study was conducted at Department of Histopathology and Cytology, Police Hospital in Khartoum State.

2.3. Study population:

Cases who were diagnosed as renal masses (neoplastic and non neoplastic) in the study area, from January 2007 up to December 2010.

2.4. Inclusion criteria:

All cases of renal masses with full records, cytological and available histological slides.

2.5 Exclusion criteria:

Cases with deficient records (missed request forms) or missed cytological slides.

2.6. Data collection:

Data were collected from the patients request forms into a pre – designed questionnaire with detailed personal, clinical and

pathological data. The slides were collected and reviewed to confirm the diagnosis of renal lesions, and to correlate the cytological and the histological diagnosis.

2.7. Data analysis and statistics:

The data were analyzed electronically using computer program SPSS (Statistical Package for Social Science) version 10.

Chapter Three

3- RESULTS

The total number of patients with renal lesions during the study period was 52 cases.

3-1 Characteristic of The Studied Patients:

3-1-1 Age distribution:

The age of the studied patients range from 24 years to 88 years , with a mean of 54.44 ± 15.6 years. 15.4 % were below the age of 40 years of age. The age group of high frequency was (50 - 59) years. **(Table 1).**

3-1-2 Sex distribution of the patients:

Twenty seven patients (51.9 %) were females, compared to 25 (48.1 %) were males **(Figure 1).** The male to female ratio was 1:1.1. The malignant lesions were found in 37 patients (71.1%) of which 20 (54 %) were females and 17 (46 %) were males, so the female to male ratio was 1:1.2.

3-1-3 Residence distribution of the studied population:

Concerning the residence of the patients, thirty three (63.5%) of them came from central regions including (Khartoum and the four central states), in which twenty three were malignant (69.7 %)

(Table 5). Eight (15.4 %) patients from northern region, seven (13.4 %) from the west region and only one case (1.9%) from the east. No cases registered from the south region in this study. In three patients (5.8 %) of the cases the residency was not stated in the request form **(Figure 5).**

3-2 Site Distribution of The Renal Lesion:

Figure 5 demonstrates the site of distribution of the renal lesion in the studied patients. Right sided masses was detected in 30 patients (57.7 %); in which 21 patients (70%) were malignant, 7 patients (23.3%) were benign and 2 patients show a hemorrhagic aspirate. Left sided masses was detected in 18 patients (34.6%); in which 15 patients (83.3%) were malignant and 3 patients (16.7%) were benign. Right sided masses were more common than left sided masses. No information concerning the site was given in 4 patients (7.7 %) and no bilateral tumors were recorded.

3-3 Distribution of The Clinical Symptoms Among Studied Patients :

The various clinical presentations in the studied group were shown in **(Table 3).** Forty two (80.8 %) patients had an abdominal mass. Thirteen (25 %) patients had loin pain. Seven (13.5 %) patients

had haematuria. Other presentations (including the cases in which no symptom is recorded) were observed in nine (17.3 %) patients.

3.4 Types of Radiology used with Benign versus Malignant Among The Studied Patients :

The radiological tools used in this study were ultrasound and computed tomography scan. Thirty six were done by computed tomography scan, in which 27 cases were malignant and 7 cases were benign. Sixteen cases were guided by ultrasound, in which 8 cases were benign and the other 8 cases were malignant **(Table 4)**.

3-5 Radiological Detection of Metastatic Renal Lesions Among The Studied Population:

During this study fifteen patients with metastatic lesions were detected by CT scan **(Figure 9)**; nine patients (60 %) with liver metastasis, five patients (33.3 %) with lung metastasis and only one patient (6.7 %) had psoas muscle metastasis. We found that most renal masses were $\geq$ 5 centimeters and more in diameter; ranging from (5-20 cm).

3-6 Cytopathological Characteristics of The Renal Lesions Among The Studied Population:

The vast majority of cases 37 (71.1 %) were malignant **(Figure 2)**, in which renal cell carcinoma predominated in 27patients (77.1%) followed by metastatic, Chromophobe, suprarenal and squamous cell carcinoma represented by three patients (8.6 %), two patients (5.7 %), tow patients (5.7 %), and one patient (2.9 %) respectively **(Figure7)**. The most common benign lesion in this study is the renal cyst; eight patients (47.1 %) followed by abscess; four patients (23.5 %), hemorrhagic aspirate; two patients (11.7%), Oncocytoma; one patient (5.9%), angiomyolipoma; one patient (5.9 %) and in one case (5.9%) no abnormality was detected **(Figure 6)** .

3-7 Correlation Between Histopathological and Cytological Diagnosis Among The Studied Population :

Ten patients from this study were histopathologically examined and all were diagnosed as renal cell carcinoma. Cytologically eight patients were diagnosed as renal cell carcinoma , and the other two were diagnosed as a benign condition **(Table 6).** The fine needle aspiration cytology had a sensitivity of 80%, specificity 100%, positive predictive value 100%, negative predictive value 86.7%.

Table1: Age distribution of the study population.

Age group (years)	Frequency	Percentage (%)
20 - 29	3	5.8
30 - 39	7	13.5
40 - 49	8	15.4
50 - 59	15	28.8
60 - 69	5	9.6
70 +	14	26.9
Total	**52**	**100.0**

Table 2: Age distribution among patients with renal cell carcinoma.

Age group (years)	Frequency	Percentage (%)
20 - 29	3	8.1
30 - 39	5	13.5
40 - 49	4	10.8
50 - 59	11	29.7
60 - 69	2	5.4
70 +	12	32.5
Total	**37**	**100.0**

Table 3: Clinical presentation of renal lesions among the study population.

Clinical presentation	Frequency	Percentage (%)
Abdominal mass	42	80.8
Lion pain	13	25.0
Haematuria	7	13.5
Others	9	17.3
Total	**52**	**100.0**

Table 4: Types of radiology used with benign versus malignant among the study population.

Radiology	Benign	Malignant	Others	Total
C.T	7	27	2	36
U\S	8	8	0	16
Total	**15**	**35**	**2**	**52**

Table 5: Benign versus malignant lesions among the study population in the central region. (n=33)

Types	**Frequency**	**Percentage %**
Malignant	23	69.7
Benign	10	30.3
Total	**33**	**100**

Table 6 : Correlation between histological and cytological diagnosis among the study population.

Type of diagnosis	Benign	Malignant	Total
Histology	0	10	10
Cytology	2	8	10

Figure 1 : Sex distribution of the study population.

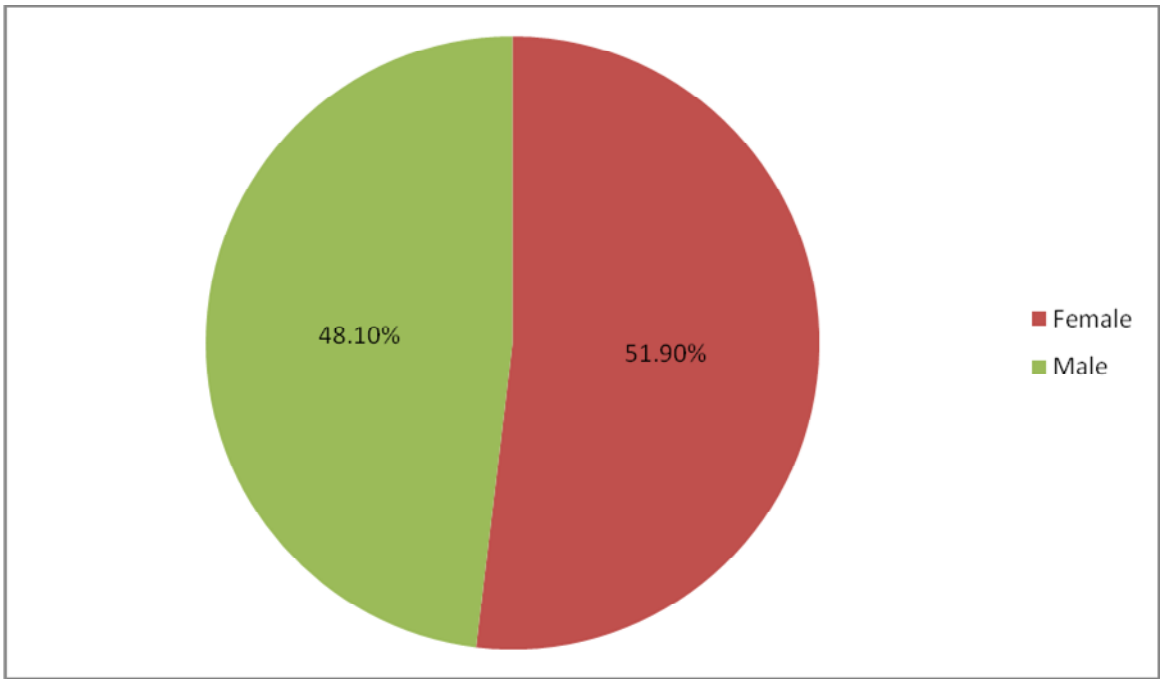

Figure 2: Benign lesions versus malignant lesions among study population.

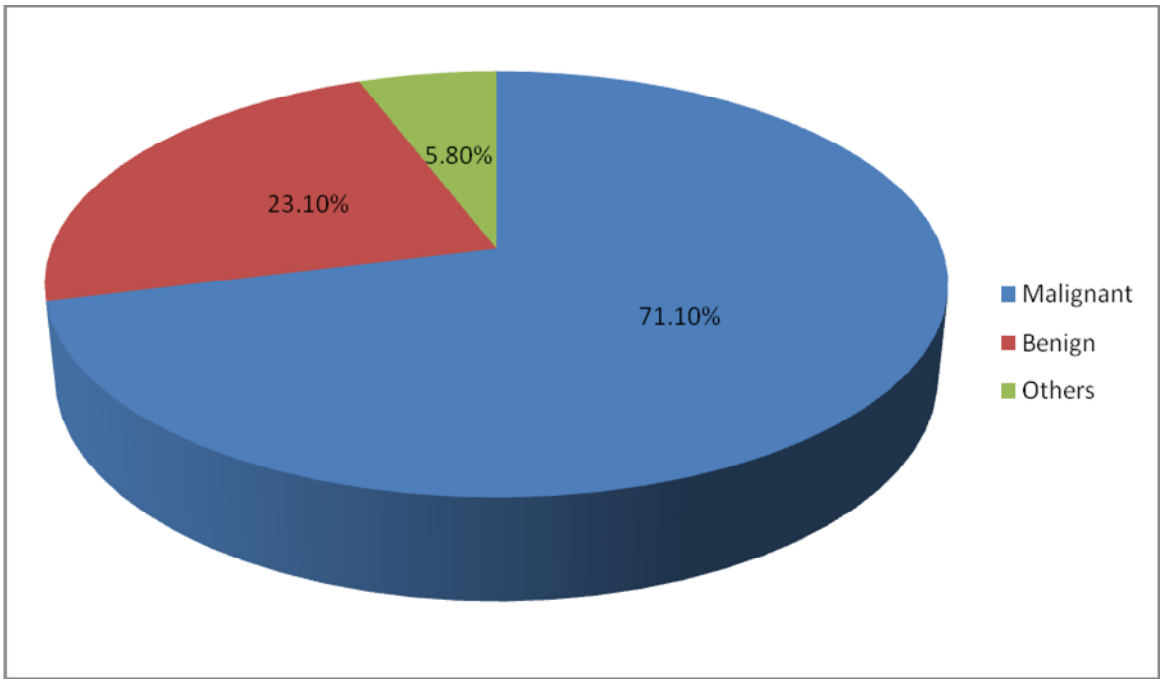

Figure 3: Sex distribution among patients with renal cell carcinoma in the study population.

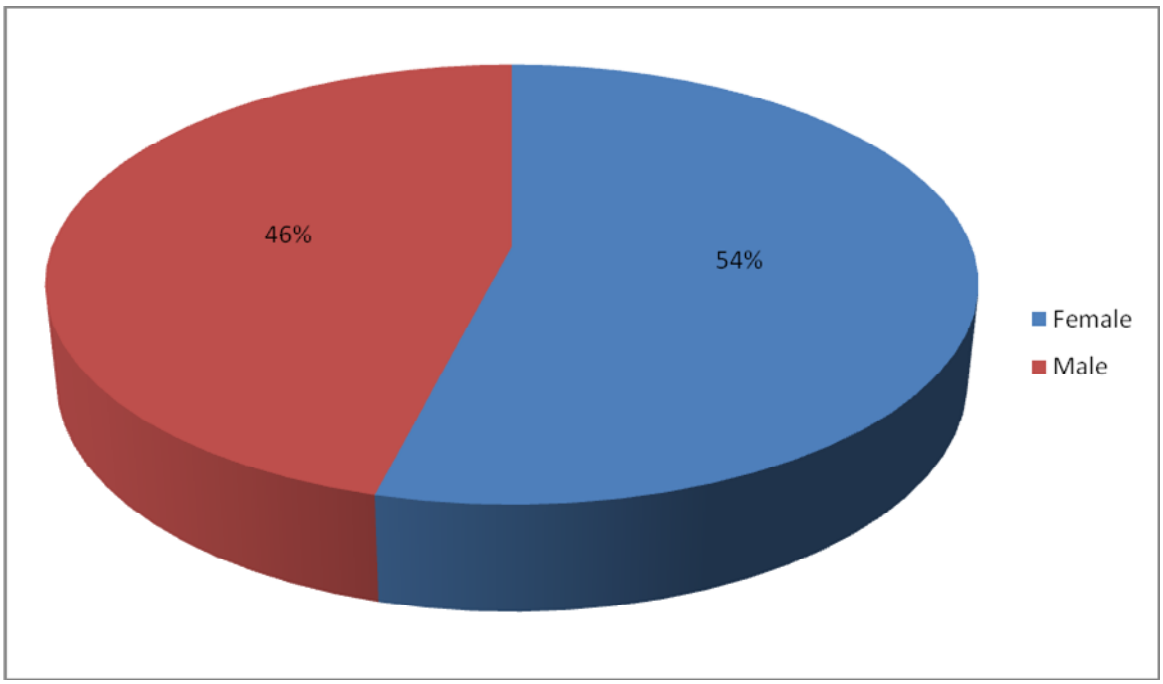

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Figure 4: Site distribution of renal masses among the study population.

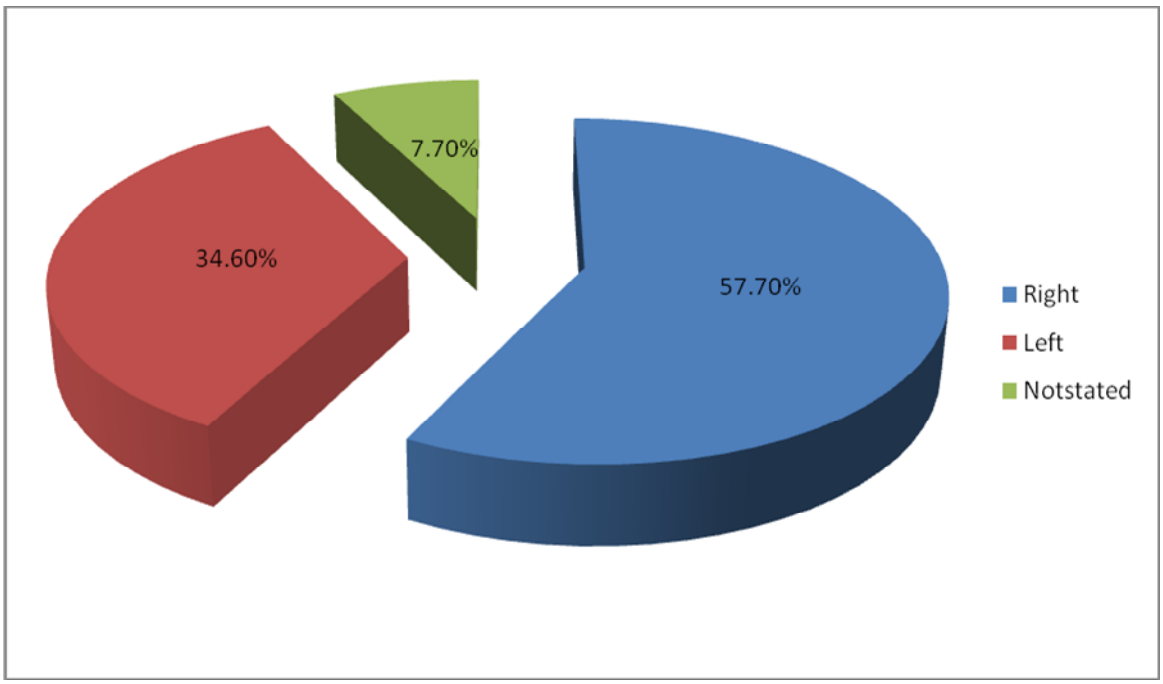


Figure 5: Distribution of the study population according to residence.

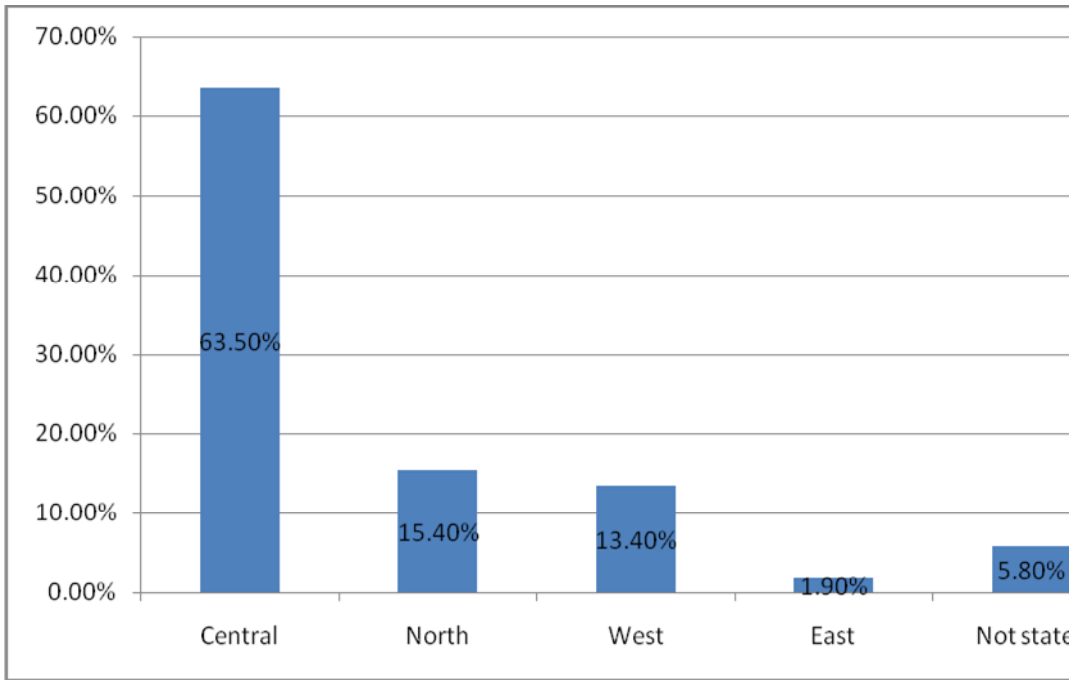


Figure 6: Cytological types of benign renal lesions among study population.

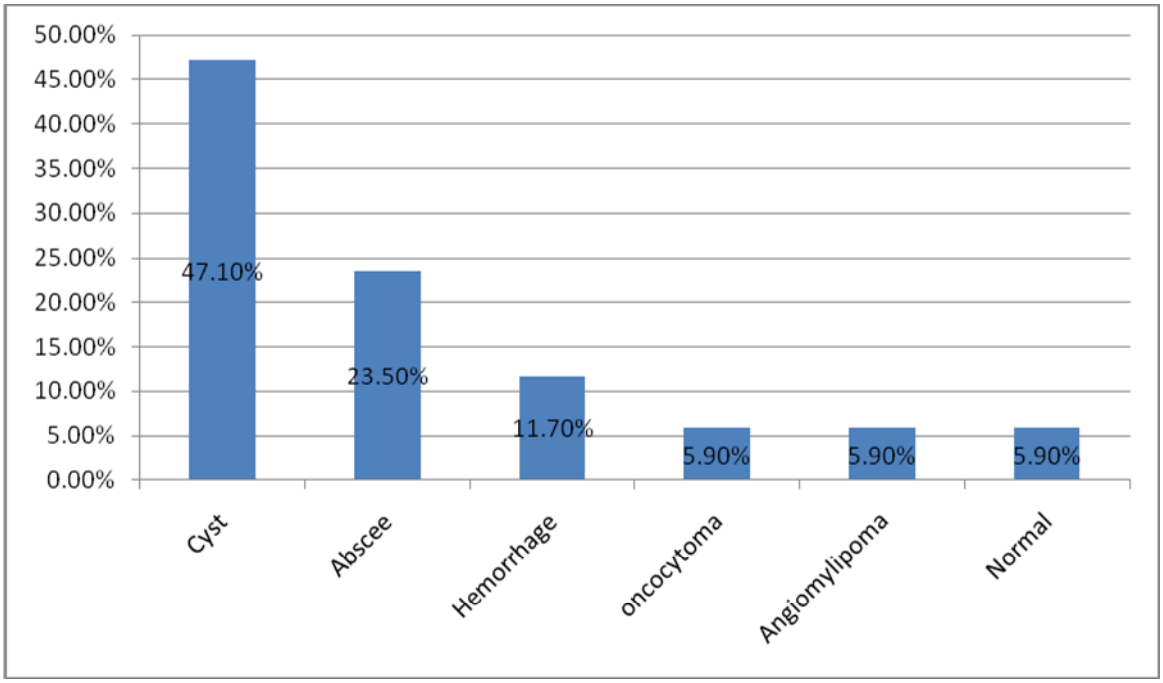


Figure 7: Cytological types of malignant renal lesions among the study population.

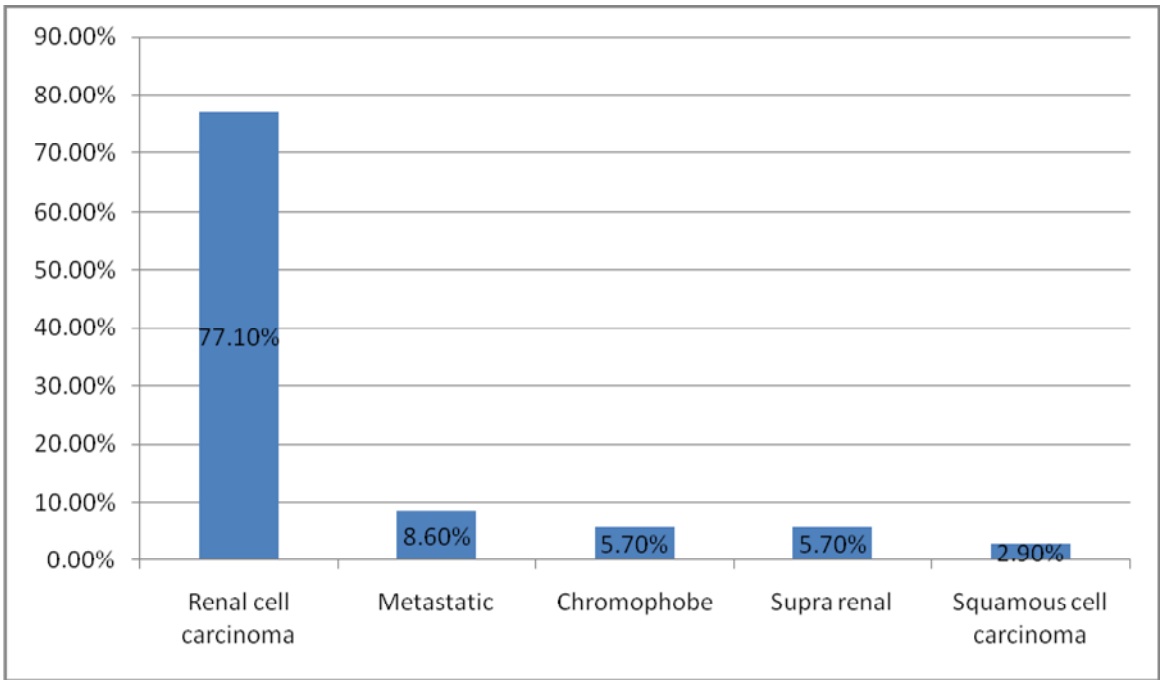
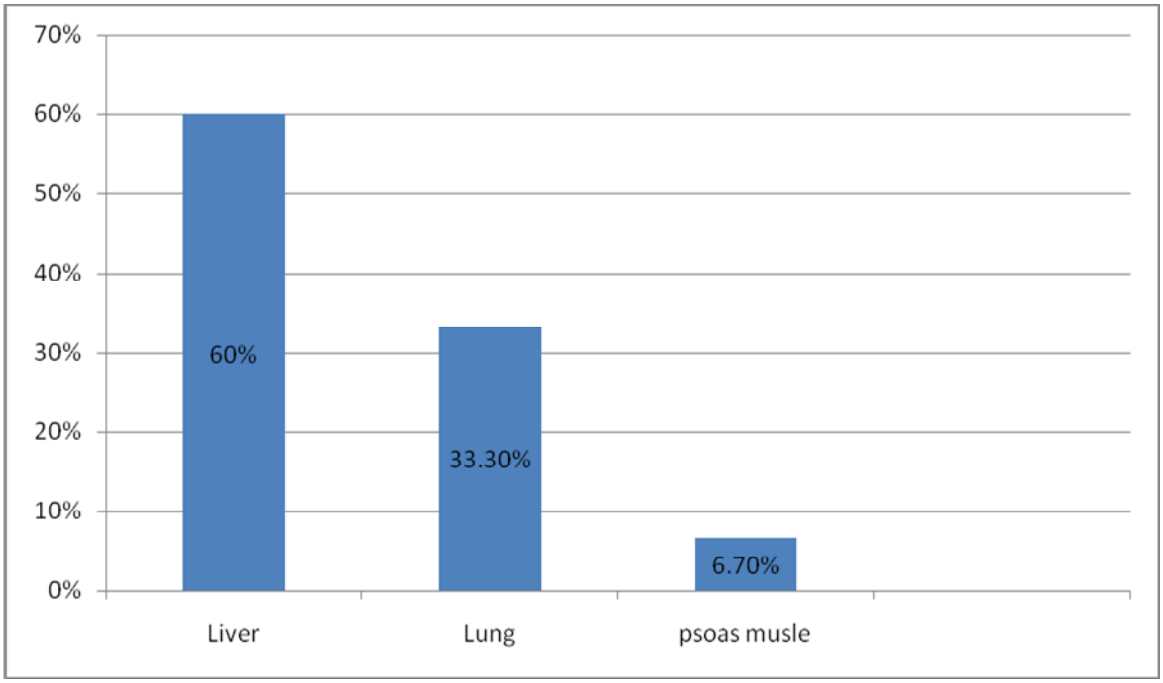


Figure 8: Radiologically detected metastatic lesions in the kidney among the study population.



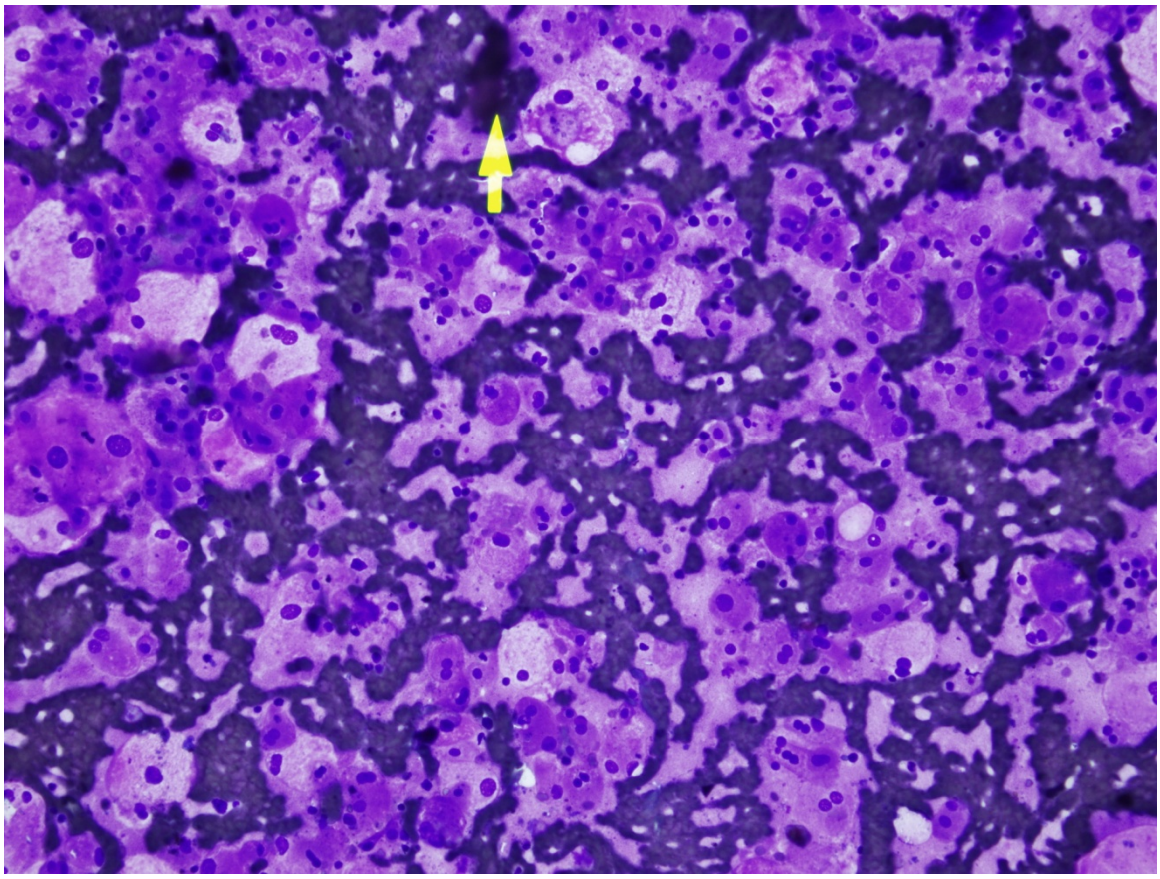


Figure 9: Chromophobe RCC; show perinuclear halo, hyperchromatic, wrinkled nuclei with frequent binucleation are present. Diff Quik, 400X

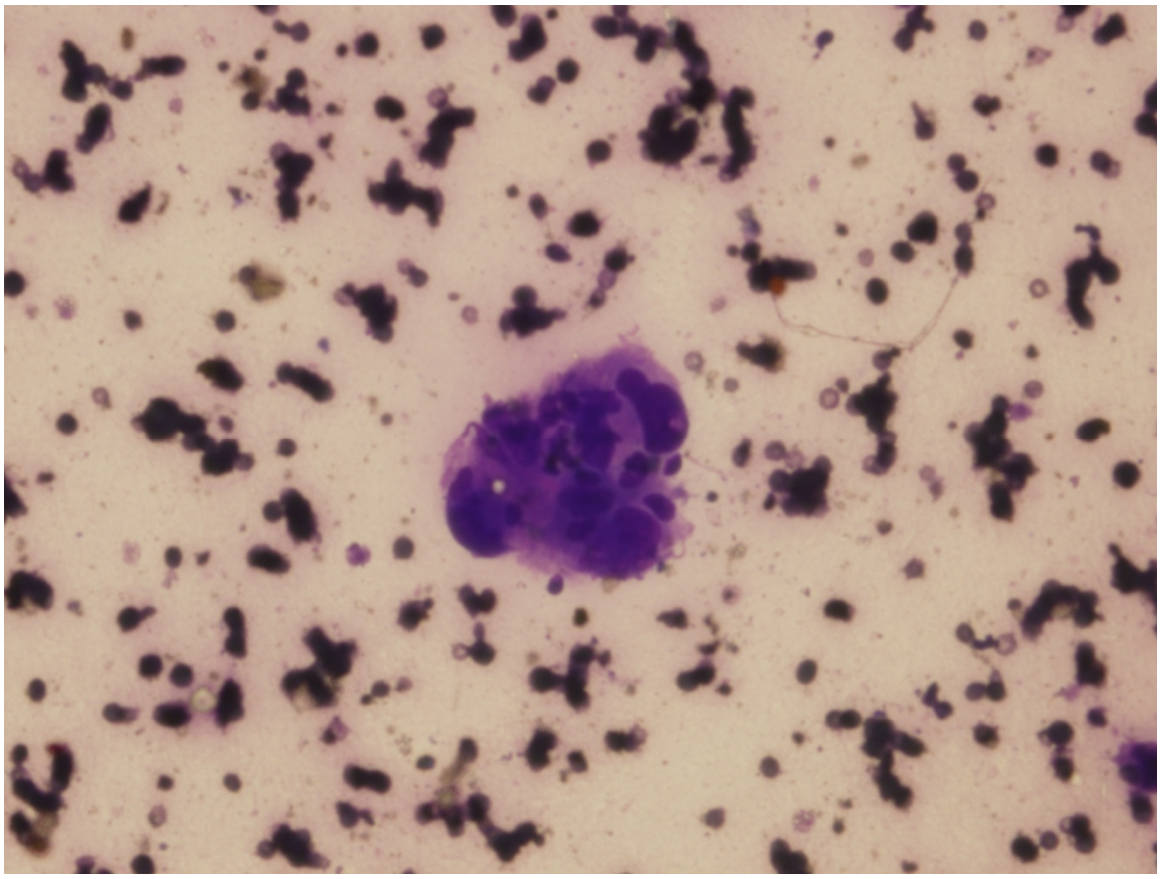


Figure 10: RCC; bizarre nuclei with macronucleoli and clumped chromatin. Diff Quik, 400X.

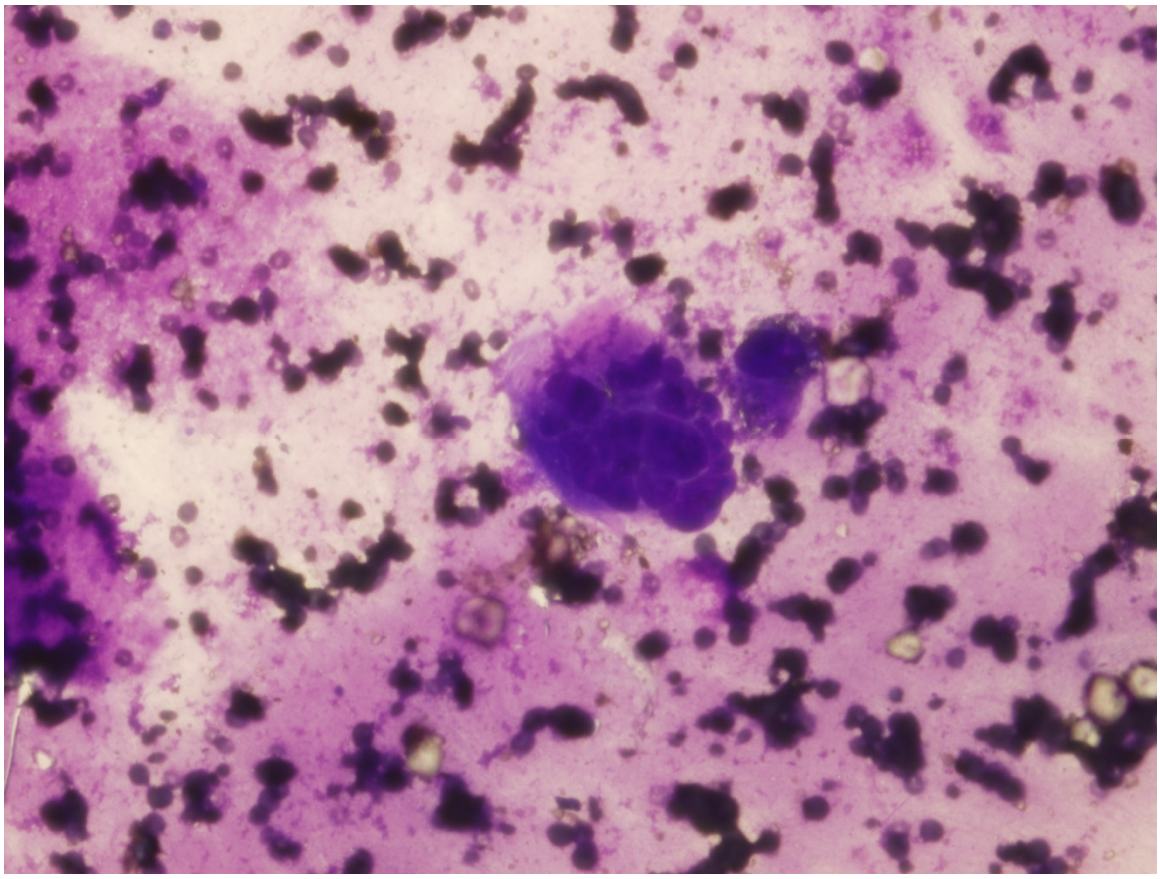


Figure 11: RCC; bizarre nuclei with macronucleoli and clumped chromatin. Diff Quik, 400X.

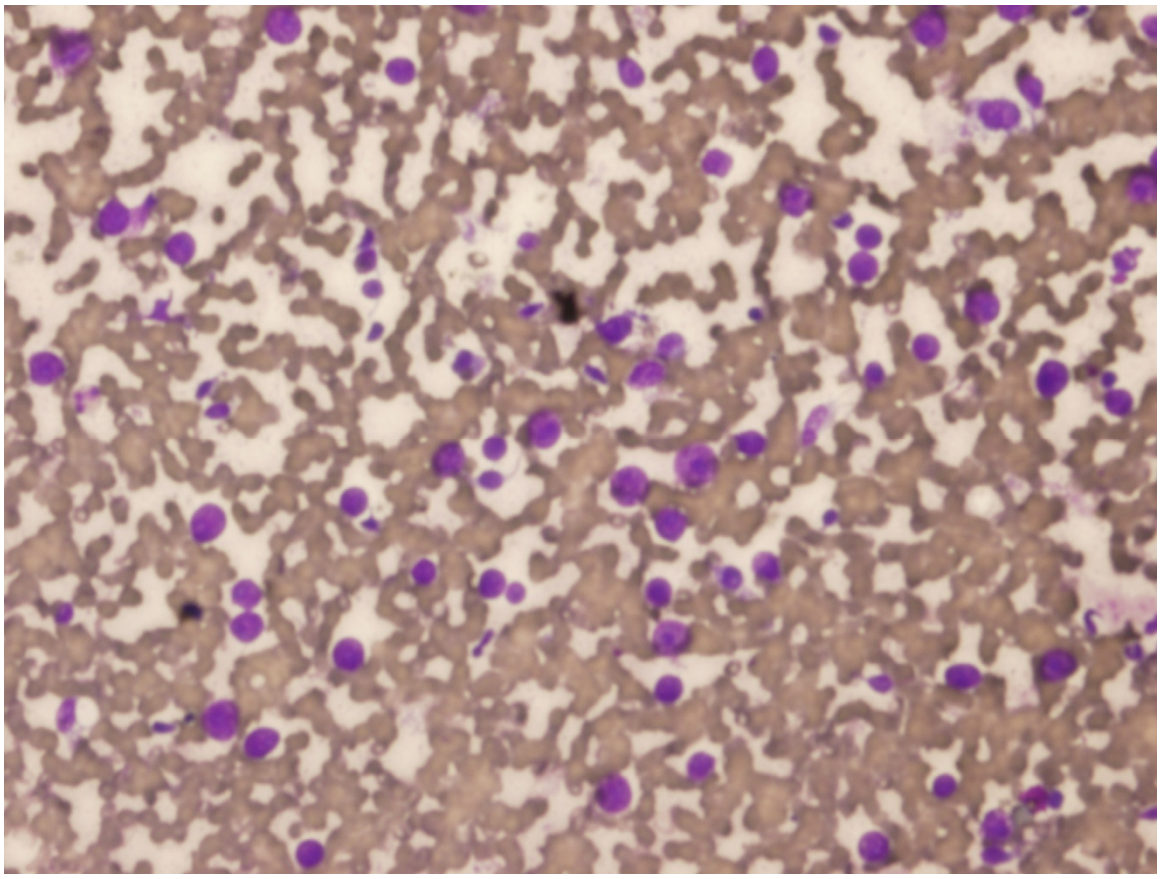


Figure 12: RCC, dyscohesive cells with prominent nucleoli . Diff Quik, 400X.

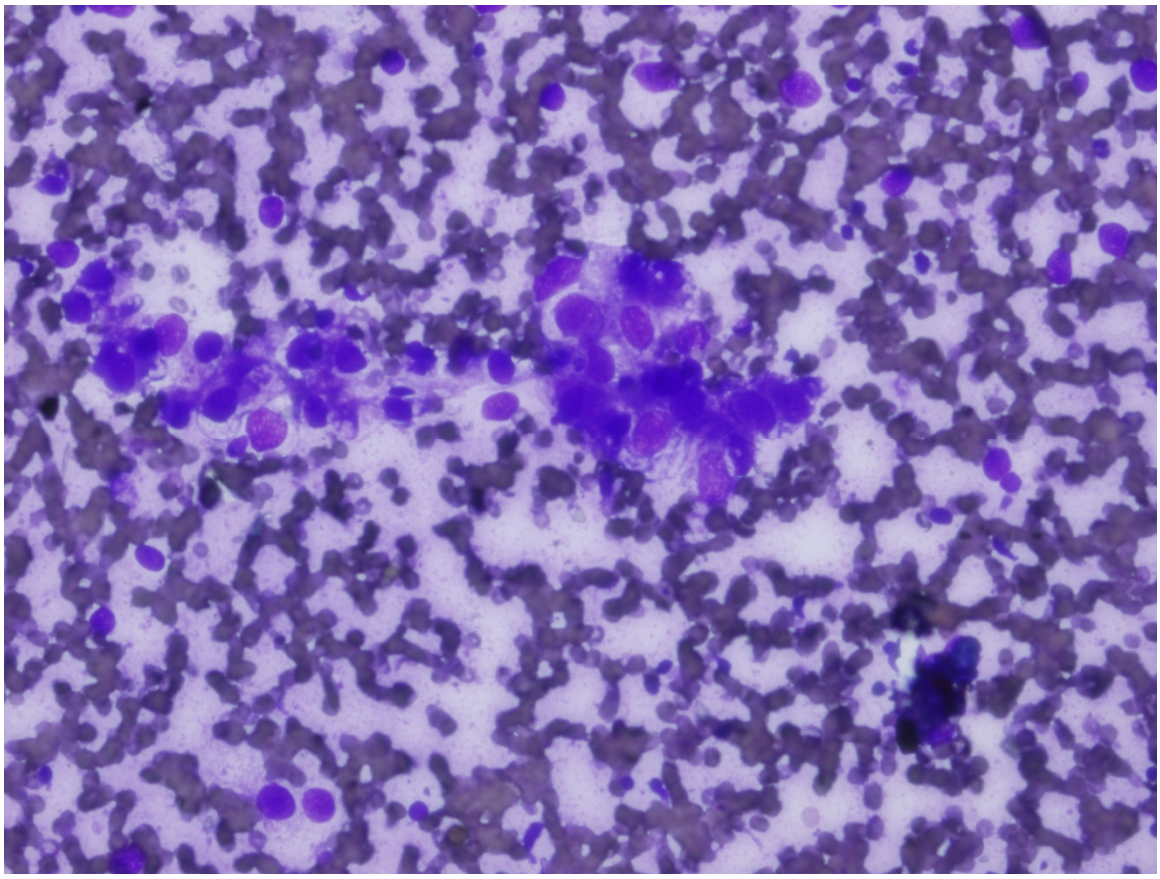


Figure 13: Conventional RCC show irregular shape nuclei with prominent nucleoli. Diff Quik, 400X.

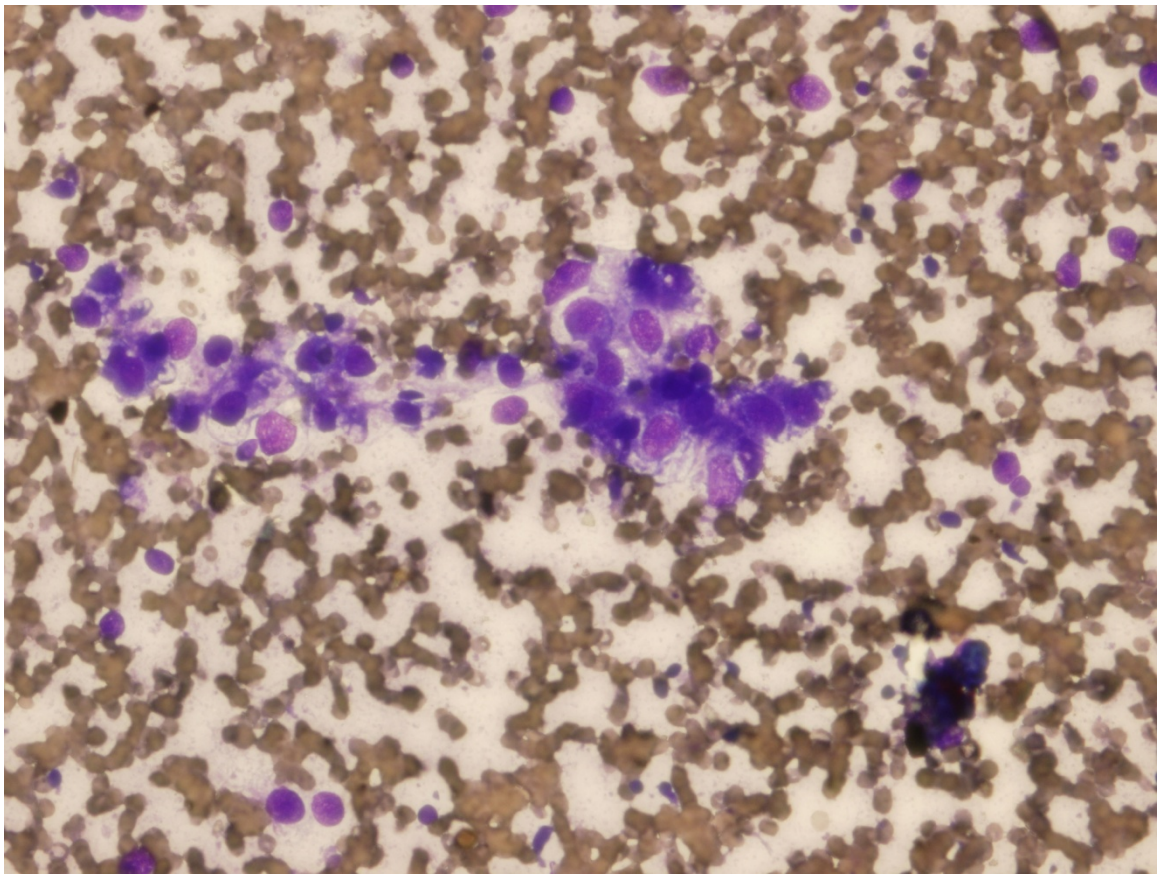


Figure 14: Conventional RCC show irregular shape nuclei with prominent nucleoli. Diff Quik, 400X.

Chapter Four

4- DISCUSSION

This study is a retrospective descriptive one to study the renal lesions in Sudanese patients . It was carried out in the period from January 2007 to December 2010 at Police hospital in Khartoum state, and includes analysis of 52 cases.

This study encountered many difficulties and limitation due to the quality of the registered data on which the study was based in particular the undetailed history and the clinical information . So caution should be taken when the result are interpreted with the international data.

The age of the patients was 24 to 88 years with the mean age of 54.4 ± 15.6 years. This is not much different from the mean age in the Western countries which was 62.0 ± 14.2 years. In addition renal lesions was found more frequent in the age 50 – 60 years , the youngest patient with renal mass was 24 years old which turned to be renal cell carcinoma and the oldest patient was 88 years old who had had a metastatic adenocarcinoma . Furthermore, (80.8 %) of the patients in our set up above the age of 40 years.

In this study females constituted (51.9 %) and males (48.1 %) with the male to female ratio 1.2:1 . Malignant lesions was detected

in 37 patients, in which 20 were females (54.1 %) and 17(45.9 %) were males, so female to male ratio is 1.2 : 1 , in contrast to Western studies, in which males are predominant and the ratio is 2-3 : 1[76].

Regarding the residence distribution, the majority (63.5 %) of the patients came from the central regions (including the capital Khartoum and the central states); in which 23 cases (69.7 %) were malignant. The least frequent place of origin being the most remote states 15.3%. This can readily be explained on the basis of demographic and economic characteristic of the Sudanese population, in that most of the Sudanese are clustered in the big towns and also unjustified focusing of the medical service in the capital. This data will agree with the studies done on breast cancer in Sudan, which show that the vast majority of patients were from Khartoum, with 43.7% in 2006, as reported by Radio Isotope centre Khartoum (RICK)[9], which is the prime centre that has prompted these services in Sudan. In addition many people in the rural areas fail to reach hospitals for diagnosis and treatment, not only because of lack of transport, but also due to their poor socioeconomic status and prevalence.

Regarding the site, the right kidney was involved in 30 patients (57.7 %), and the left in 18 (34.6 %), so the right side was more

common. This is similar to the study done by Santosh Kumar, in which the right side was common.[75]

Regarding clinical presentation 42 (80.9 %) presented with abdominal mass, while 13 (25 %) with loin pain , 7 (13.5 %) with haematuria. In 6 patients no data was available. This is different from study done in Western countries; where most patients came with haematuria (60%), loin pain (40%), abdominal mass (25%)[78]. This difference can be explained by the incomplete registered data and deficient history and clinical information.

During this study with supporting evidence of radiology we had 15 patients with a metastatic renal cell carcinoma. Nine patients (60%) to the lung, 5 patient (913.3%) to the liver and only one (6.7%) to the psoas muscle **(Figure 8).** This results do not agree with the literatures in which the lung is the commonest site (75%) followed by soft tissue (36%) bone (20%) liver (18%) [76]. The tumor size varied from 6 centimeters up to 20 centimeters in diameter, in which (63%) were above 10 centimeters by radiological detection.

Cytological studies showed that the commonest malignant tumor diagnosed was conventional renal cell carcinoma (77.1%) **(Figure 7)** . The cytological features and the percentage of

malignancy were consistent with the finding of Renshaw et al. [73- 75] Also we had two cases (5.7 %) of chromophobe renal cell carcinoma. The cytologic features corresponded well with the histopathologic picture, including cytoplasmic and nuclear characteristics, these cytoplasmic features are similar to those in what to our knowledge are the relatively few cases described in the literature [76,77] and correspond particularly well with the cases described most recently by Granter and Renshaw.[77]

Histopathological investigation results were available in 10 cases. All cases were diagnosed as renal cell carcinoma of clear cell type by histopathology. Two cytological cases were inconsistent with the histological diagnosis **(Table 3)**. One case was misdiagnosed as oncocytoma on cytology. The aspirates of predominantly granular cell conventional renal cell carcinoma are more difficult to interpretate, because cells with granular cytoplasm are present in oncocytoma, eosinophilic chromophobe carcinoma. [76, 80, 81] In this case the needle may take the sample from the granular area. The second case was the cytologically diagnosed just a hematoma.

The sensitivity obtained was thus 80%, along with specificity of 100%. This finding was slight lower to the sensitivity and

specificity obtained by Bezabih were lower: 88.5% and 81.5% respectively.

Conclusion

Radiologically-guided FNAC is an inexpensive, simple, rapid, safe, had high specificity and low sensitivity for the diagnosis of renal masses.

In this study we have a greater incidence in the age of 50 to 60 years and the malignant lesions are more common than the benign lesions, but differ in sex; female more common than male and the clinical presentation compared to Western studies.

The study identified five cytological and histological types of malignant kidney masses, namely; conventional renal cell carcinoma, chromophobe renal cell carcinoma, squamous cell carcinoma, supra renal and metastatic to the kidney.

Cytopatholohical correlation was available in 10 cases, all diagnosed as renal cell carcinoma and we have two cytological diagnosis were inconsistent with histological diagnosis.

RECOMMENDATIONS

- Further studies with an increase number of histological correlation are recommended.
- Special attention should be paid to the disproportional high rate of renal malignant lesions in patients from the central region . Further demographical and environmental studies are highly recommended in that part of the country.
- Improvement of cancer reporting and registration activities.

Reference

REFERENCES

1) Orel SR, longlois SLP, Marshal VP. (1985) Fine _ needle aspiration cytology in the diagnosis of solid renal and adrenal masses. Scand J Urol Nephron 19:211–216.

2) Jornoza J, Handed P, Lukeman JM, et al. (1977) Percutaneous transperitoneal biopsy in urologic malignancies. Urology 9:395–398.

3) Nguyen GK. (1987) Percutaneous fine _ needle aspiration cytology of kidney and adrenal. Patho Annu 22: 163-164 (part 1) .

4) Tao LC, Pearson FG, Delarue NC, et al. (1980) Percutaneous fine – needle aspiration biopsy:1.Its value to clinical practice. Cancer 45 :1480 - 1485.

5) Tao LC, Sanders D, McLoughlin ML, et al. (1980) Current concept in fine - needle aspiration biopsy cytology. Hum Pathol 11:93–94.

6) Bret PM, Fone A, Casola G. (1986) Abdominal lesions: Aprospective study of clinical efficacy of percutaneous fine-needle biopsy. Radiology 159:345–346.

7) Grace Chia – yu, Hsu Yang, Liang - Ch Tao.(2007) Transabdominal fine needle Biopsy. Second Edition. p 4-7

8) McLaughlin JK, Lipworth L: Epidemiologic aspects of renal cell cancer. Semin Oncol 2000; 27:115.

9) Annual Reports from Department of Medical Statistics and Registrations, Radioisotopes centre of Khartoum, 200-2010.

10) Stanley L, Robbin, Ramzi S, Cortan.(2007) Pathological Bases of Disease, Seventh edition; 20: 1015.

11) Walter F., PhD. Boron (2004). Medical Physiology: A Cellular and Molecular Approach. Elsevier/Saunders. ISBN 1-4160-2328-3.

12) Walter F., PhD. Boron (2004). Medical Physiology: A Cellular and Molecular Approach. Elsevier/Saunders. ISBN 1-4160-2328-3.

13) Bard, Johnathan; Vize, Peter D.; Woolf, Adrian S. (2003). The kidney: from normal development to congenital disease. Boston: Academic Press. pp. 154. ISBN 0-12-722446.HTTP://BOOKS.GOOGLE.COM/?ID=CTOM-cPwo60C&pg=PA154.

14) Koss LG,Woyke S, OlszewskiW. (1992) Aspiration Biopsy: Cytologic Interpretation and Histologic Bases. Philadelphia, LippincottWilliams &Wilkins.

15) Plowden KM, ErozanYS, Frost JK. (1984) Cellular atypia associated with bengin lesions of the kidney as seen as fine needle aspirates. Acta Cytol 28:648.

16) Pollack HM, Banner MP, Arger PH, et al. (1982) The accuracy of gray-scale renal ultrasonography in differentiating cystic neoplasms from benign cysts. Radiology 143:741–745.

17) Conrad MR, Sanders RC, Mascardo AD. (1977) Perinephric abscess aspiration using ultrasound guidance. Am J Roentgenol 128:459–464.

18) Grace Chia- yu, Hsu Yang, Liang - che Tao.(2007) Transabdominal fine needle biopsy, 2nd edition; 6:169.

19) Eble JN. (1998) Angiomyolipoma of kidney. Semin Diagn Pathol 15:21–40.

20) Panizo-Santos A, Sola I, de Alava E, et al. (2003) Angiomyolipoma and PEComa are immunoreactive for MyoD1 in cell cytoplasmic staining pattern. Appl Immunohistochem Mol Morphol 11:156–160.

21) Ashfaq R,Weinberg AG, Alboressaavedra J. (1993) Renal angiomyolipomas and HMB-45 reactivity. Cancer 71:3091–3097.

22) Lingeman JE, Donohue JP,Madura JA, et al. (1982)Angiomyolipoma: Emerging concepts in management. Urology 20:566–570.

23) Glenthoj A, Parrott S. (1984) Ultrasound-guided percutaneous aspiration of renal angiomyolipoma. Acta Cytol 28:265–268.

24) Nguyen GK. (1984) Aspiration biopsy cytology of renal angiomyolipoma. Acta Cytol 28:261–264.

25) Barrilero AE. (1977) Renal angiomyolipoma: A study of 13 cases. J Urol 117:547–552.

26) Renshaw AA, Maurici D, Fletcher JA. (1997) Cytologic and fluorescence in situhybridization (FISH) examination of metanephric adenoma. Diagn Cytopathol 16:107–111.

27) Pierson CR, Schober MS, Wallis T, et al. (2001) Mixed epithelial and stromal tumor of the kidney lacks the genetic alterations of cellular congenital mesoblastic nephroma. Hum Pathol 32:513–520.

28) KleinMJ,Valensi QJ. (1976) Proximal tubular adenoma of kidney with so-called oncocytic features. Cancer 38:906–914.

29) Lieber MM, Tomera KM, Farrow GM. (1981) Renal oncocytoma. J Urol 125: 481–485.

30) Liu J, Fanning CV. (2001) Can renal onococytomas be distinguished from renal cell carcinoma on fine-needle aspiration specimens. Cancer (Cancer Cytopathol) 93:390–397.

31) Wiatrowska BA, Zakowski ME. (1999) Fine-needle aspiration of chromophobe renal cell carcinoma and oncocytoma: Comparison of morphologic features. Cancer (Cancer Cytopathol) 87:161–167.

32) Reuter VE,Tickoo SK. (2004)Adult renal tumors. In:Mills SE, et al. (eds.),Sternberg's Diagnostic Surgical Pathology, 4th ed. New York, Lippincott Williams Wilkins.

33) Meisels A. (1963) Cytology of carcinoma of the kidney. Acta Cytol 7:239–244.

34) Suen KC. (1988) Guides to Clinical Aspiration Biopsy: Retroperitoneum and Intestine. New York, Igaku-Shoin.

35) Yang GCH, Hoda SA. (1997) Combined use of “scratch and smear” sampling technique and Ultrafast Papanicolaou stain for intraoperative cytology. Acta Cytol 41:1315–1318.

36) Crotty TB, Lawrence KM, Moertel CA, et al. (1992) Cytogenetic analysis of six renal oncocytomas and a chromophobe cell renal carcinoma. Evidence that - Y, - 1 may be a characteristic anomaly in renal oncocytomas. Cancer Genet Cytogenet 61:61–66.

37) Wiatrowska BA, Zakowski ME. (1999) Fine-needle aspiration of chromophobe renal cell carcinoma and oncocytoma: Comparison of morphologic features. Cancer (Cancer Cytopathol) 87:161–167.

38) Delahunt B, Eble JN. (1997) Papillary renal cell carcinoma: A clinicopathologic and immunohistochemical study of 105 tumors. Mod Pathol 10:537–544.

39) Delahunt B, Eble JN,McCredie MRE, et al. (2001)Morphologic typing of papillary renal cell carcinoma: Comparison of growth kinetics and patient survival in 66 cases. Hum Pathol 32:590–595.

40) Granter SR, Perez-Atayde AR, Renshaw AA. (1998) Cytologic analysis of papillary renal cell carcinoma. Cancer (Cancer Cytopathol) 84:303–308.

41) Kovacs G, Fuzesi L, Emanual A, Kung HF. (1991) Cytogenetics of papillary renal cell tumors. Genes Chromos Cancer 3:249–255.

42) Thoenes W, Storkel S, Rumpelt H-J. (1995) Human chromophobe renal cell carcinoma. Virchows Arch B Cell Pathol 48:207–217.

43) Kuroda N, Toi M, Hiroi M, Enzan H. (2003) Review of chromophobe renal cell carcinoma with focus on clinical and pathobiological aspects. Histol Histopathol 18:165–171.

44) Granter SR, Renshaw AA. (1997) Fine-needle aspiration of chromophobe renal cell carcinoma. Analysis of six cases. Cancer (Cancer Cytopathol) 81:122–128.

45) Fleming S, Lewi HJE. (1986) Collecting duct carcinoma of the kidney. Histopathology 10:1131–1141.

46) Ham AW. (1974) Histology, 7th ed. Philadelphia, J.B. Lippincott Co.

47) Layfield LJ. (1994) Fine-needle aspiration of renal collecting duct carcinoma. Diagn Cytopathol 11:74–78.

48) Auger M, Katz RL, Sella A, et al. (1993) Fine-needle aspiration of sarcomatoid renal cell carcinoma. A morphologic and immunohistochemical analysis of 15 cases. Diagn Cytopathol 9:45–51.

49) Nurmi M, Tyrkko J, Puntala P, et al. (1984) Reliability of aspiration biopsy cytology in the grading of renal adenocarcinoma. Scand J Urol Nephrol 18: 155–156.

50) Rosai J. (2004) Rosai and Ackerman's Surgical Pathology, 9th ed. St. Louis, CV Mosby.

51) Powers CN, Elbadawi A. (1995) "Cercariform" cells: A clue to the cytodiagnosis of transitional cell origin of metastatic neoplass? Diagn Cytopathol 13:15–21.

52) Farrow GM, Harrison EG Jr, Utz DC, et al. (1968) Sarcomas and sarcomatoid and mixed malignant tumors of the kidney in adults. Cancer 22:545–550.

53) Wong JY, Zaharopoulos P. (1983) Cytologic features on needle aspiration of Wilms' tumor in an adult: A case report. Acta Cytol 27:67–72.

54) Li P, Perle MA, Scholes JV,Yang GCH. (2002)Wilms' tumor in adults:Aspiration cytology and cytogenetics. Diagn Cytopathol 26:99–103.

55) Kilton L, Matthews MJ, Cohen MH. (1980) Adult Wilms' tumor: A report of prolonged survival and review of literature. J Urol 124:1–5.

56) Bray G, Pendergrass TW, Schaller RT Jr, et al. (1986) Preoperative chemotherapy in the treatment of Wilms' tumor diagnosed with the aid of fine-needle aspiration biopsy. Am J Pediatr Hematol Oncol 8:75–78.

57) Leape LL. (1978) Diagnosis and management ofWilms' tumors and neuroblastomas. In: SkinnerDG, deKernion JB (eds.),Genitourinary Cancer. Philadelphia,WB Saunders.

58) Jemal, A, Siegel, R, Xu, J, Ward, E. Cancer statistics,2010. CA Cancer J Clin 2010, 60:277.

59) Ferlay J, Shin HR, Bray F, Forman D, et al. GLOBOCAN 2008 Cancer Incidence and Mortality Worldwide: IARC CancerBase No . 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010.Available from: http://globocan.iarc.fr

60) Parkin, DM, Pisani, P, Ferlay, J. Estimates of the worldwide incidence of eighteen major cancers in 1985. Int J Cancer 1993; 54:594.

61) Kosary, CL, McLaughlin, JK. Kidney and renal pelvis. Ries, LAG, Hankey, BF, et al. (Eds), Natl Cancer Inst, Bethesda 1993. (NIH publication no. 93-2789, XL.IXI.22).

62) Kosary, CL, McLaughlin, JK. Kidney and renal pelvis. Ries, LAG, Hankey, BF, et al. (Eds), Natl Cancer Inst, Bethesda 1993. (NIH publication no. 93-2789, XL.IXI.22).

63) Kosary, CL, McLaughlin, JK. Kidney and renal pelvis. Ries, LAG, Hankey, BF, et al. (Eds), Natl Cancer Inst, Bethesda 1993. (NIH publication no. 93-2789, XL.IXI.22).

64) Nguyen, MM, Gill, IS, Ellison, LM. The evolving presentation of renal cell carcinoma in United States: trends from the Surveilllance, Epidemiology, and End Result program. J Urol 2006; 176:2397.

65) Stafford, HS,Saltzstein, JL, Shimasaki, S, et al. Racial/ ethnic and gender disparities in renal cell carcinoma incidence and survival. J Urol 2008; 179: 1704.

66) Cooperberg, MR, Mallin, K, Ritchey, J, et al. decreasing size at diagnosis of stage 1 renal cell carcinoma: analysis from the National Cancer Data Base; 1993 to 2004. J Urol 2008; 179: 2131.

67) Kane, CJ, Mallin, K, Ritchey, J, et al. Renal cell cancer stage migration: analysis of the Natinal Cancer Data Base. Cancer 2008; 113:78.

68) Lipworth L, Tarone RE, McLaughlin JK (December 2006). "The epidemiology of renal cell carcinoma". J. Urol. 176 (6 Pt 1): 2353–8. doi:10.1016/j.juro.2006.07.130. PMID 17085101

69) Brennan JF, Stilmant MM, Babayan RK, Siroky MB (April 1991). "Acquired renal cystic disease: implications for the urologist". Br J Urol 67 (4): 342–8. doi:10.1111/j.1464-410X.1991.tb15158.x. PMID 2032071.

70) McLaughlin JK, Kidney Cancer, Oxford University Press, Oxford, 2006, pp. 1087–1100.

71) Lamiell JM, Salazar FG, Hsia YE (January 1989). "von Hippel-Lindau disease affecting 43 members of a single kindred". Medicine (Baltimore) 68 (1): 1–29. PMID 2642584.

72) Fuhrman S, Lasky L, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. *Am J Surg Pathol* 1982;6:655–63.

73) Taxy JB, Marshall FF. Multilocular renal cysts in adults. Arch Pathol Lab Med 1983;107:633–7.

74) Koss LG. Diagnostic cytology of the urinary tract. Philadel phia: Lippincott-Raven, 1995.

75) van den Berg E, van der Hout AH, Oosterhuis JW, Storkel S, Dijhuizen T, Dam A, et al. Cytogenetic analysis of epithelial renal-cell tumors: relationship with a new histopathological classification. Int J Cancer 1993;55:223–7.

76) Helm CW, Burwood RJ, Harrison NW, Melcher DH. Aspiration cytology of solid renal tumors. J Urol 1983;55:249–53.

77) Dekmezian RH, Charnsangavej C, Rava P, Katz RL. Fine neeCytopadle aspiration of kidney tumors in 105 patients: a cytologic and histologic correlation [abstract]. Acta Cytol 1985;29:931.

78) Murphy WM, Zambroni BR, Emerson LD, Moinuddin S, LeeLH. Aspiration biopsy of the kidney. Cancer 1985;56:200–5.

79) Renshaw AA, Lee KR, Madge R, Granter SR. Accuracy of fine needle aspiration in distinguishing subtypes of renal cell carcinoma. Acta Cytol. In press.

80) Plowden KM, Erozan YS, Frost JK. Cellular atypias associated with benign lesions of the kidney as seen in fine needle aspirates [abstract]. Acta Cytol 1984;28:6489

81) Shuin T, Kondo K, Torigoe S, Kishida T, Kubota Y, Hosaka M, et al. Frequent somatic mutations and loss of heterozy gozity of the von Hippel-Lindau tumor suppressor gene in primary human renal cell carcinoma. Cancer Res 1994; 54:2852–5.

Appendix

University of Khartoum

Faculty of Medicine

Postgraduate Medical Studies Board

Questionnaire

The role of radiologically guided fine needle aspiration cytology in the diagnosis of renal masses.Clincopathological study

Date_____ Lab.Number:_____

Personal data:

Name:_____

Sex:_____

Age:_____ Residence:_____

Clinical data:

Renal mass: Site:_____

Duration:_____ Pain:_____

Haematuria: _____ Others:_____

Investigations:

Radiology

:U/S:___+_____

CT:_____

Cytological Finding:_____

Microscopy:_____

Histological Finding:

Gross: Specimen (type of operation):_____

Description:_____

Microscopy:_____

WHO Histological Classification of Tumors of The Kidney:

Renal cell tumors:

- Clear cell renal cell carcinoma 8310/31
- Multilocular clear cell renal cell carcinoma 8310/3
- Papillary renal cell carcinoma 8260/3
- Chromophobe renal cell carcinoma 8317/3
- Carcinoma of the collecting ducts of Bellini 8319/3
- Renal medullary carcinoma 8319/3
- Xp11 translocation carcinomas
- Carcinoma associated with neuroblastoma
- Mucinous tubular and spindle cell carcinoma
- Renal cell carcinoma, unclassified 8312/3
- Papillary adenoma 8260/0
- Oncocytoma 8290/0

Metanephric tumors:

- Metanephric adenoma 8325/0
- Metanephric adenofibroma 9013/0
- Metanephric stromal tumour 8935/1

Nephroblastic tumors:

- Nephrogenic rests

- Nephroblastoma 8960/3
- Cystic partially differentiated nephroblastoma 8959/1

Mesenchymal tumors:

Occurring Mainly in Children

- Clear cell sarcoma 9044/3
- Rhabdoid tumour 8963/3
- Congenital mesoblastic nephroma 8960/1
- Ossifying renal tumour of infants 8967/0

Occurring Mainly in Adults:

- Leiomyosarcoma (including renal vein) 8890/3
- Angiosarcoma 9120/3
- Rhabdomyosarcoma 8900/3
- Malignant fibrous histiocytoma 8830/3
- Haemangiopericytoma 9150/1
- Osteosarcoma 9180/3

§ Angiomyolipoma 8860/0

- Epithelioid angiomyolipoma
- Leiomyoma 8890/0
- Haemangioma 9120/0
- Lymphangioma 9170/0
- Juxtaglomerular cell tumour 8361/0

- Renomedullary interstitial cell tumour 8966/0
- Schwannoma 9560/0
- Solitary fibrous tumour 8815/0

Mixed Mesenchymal and epithelial tumors

- Cystic nephroma 8959/0
- Mixed epithelial and stromal tumour
- Synovial sarcoma 9040/3

Neuroendocrine tumors:

- Carcinoid 8240/3
- Neuroendocrine carcinoma 8246/3
- Primitive neuroectodermal tumour 9364/3
- Neuroblastoma 9500/3
- Phaeochromocytoma 8700/0

Haematopoietic and lymphoid tumors:

- Lymphoma
- Leukaemia
- Plasmacytoma 9731/3

Germ cell tumors:

- Teratoma 9080/1
- Choriocarcinoma 9100/3

Metastatic tumors

TNM Classification:

Primary Tumour:

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour
- T1 Tumor 7 cm or less in greatest dimension, limited to the kidney
- T1a Tumor 4 cm or less
- T1b Tumor more than 4 cm but not more than 7 cm
- T2 Tumour more than 7 cm in greatest dimension, limited to the kidney
- T3 Tumor extends into major veins or directly invades adrenal gland or perinephric tissues but not beyond Gerota fascia
- T3a Tumor directly invades adrenal gland or perinephric tissue but not beyond Gerota fascia
- T3b Tumor grossly extends into renal vein(s) b or vena cava or its wall below diaphragm.
- T3c Tumor grossly extends into vena cava or its wall above diaphragm
- T4 Tumor directly invades beyond Gerota fascia

Notes: a Includes renal sinus (peripelvic) fat b Includes segmental (muscle - containing) branches.

N - Regional Lymph Nodes:

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in a single regional lymph node
- N2 Metastasis in more than one regional lymph node

M-Distant Metastasis:

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis.